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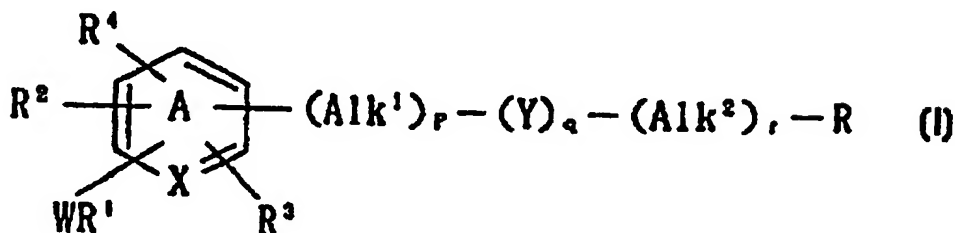
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(54) **COMPOSES CHIMIQUES ET UTILISATION
PHARMACEUTIQUE**

(54) **NOVEL COMPOUNDS AND PHARMACEUTICAL USE
THEREOF**



(57) La présente invention concerne des composés représentés par la formule générale (I) et certains de leurs sels galéniques. Dans cette formule, chaque symbole correspond à la définition qui en est donnée dans la spécification. Ces composés et sels, agissant sélectivement sur les récepteurs des cannabinoïdes, spécialement les récepteurs périphériques, présentent de moindres effets secondaires au niveau du système nerveux central et conviennent particulièrement aux traitements immunomodulateurs, anti-inflammatoires et anti-allergiques. Ils sont en outre efficaces en thérapie anti-néphritique. Il en résulte qu'ils conviennent comme agonistes et antagonistes des récepteurs des cannabinoïdes (spécialement les récepteurs périphériques des cannabinoïdes), comme immunomodulateurs, comme remèdes contre les maladies auto-immunes, comme anti-inflammatoires, comme anti-allergiques et comme anti-néphritiques.

(57) Compounds represented by general formula (I) and pharmaceutically acceptable salts thereof: wherein each symbol is as defined in the specification. These compounds and salts act selectively on cannabinoid receptors, especially peripheral receptors, are reduced in the side effects against the central nervous system, and are excellent in immunomodulatory, anti-inflammatory and antiallergic activities and a nephritis curing effect, thus being useful as agonists and antagonists of cannabinoid receptors (especially peripheral cannabinoid receptors), immunomodulator, remedies for autoimmune diseases, anti-inflammatory, antiallergic, and nephritis remedy.



-PCT

特許協力条約に基づいて公開された国際出願



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<p>(21) 国際出願番号 PCT/JP97/00291</p> <p>(22) 国際出願日 1997年2月6日(06.02.97)</p> <p>(30) 優先権データ 特願平8/20083 1996年2月6日(06.02.96) JP 特願平8/94989 1996年4月17日(17.04.96) JP</p> <p>(71) 出願人 (米国を除くすべての指定国について) 日本たばこ産業株式会社(JAPAN TOBACCO INC.)(JP/JP) 〒105 東京都港区虎ノ門二丁目2番1号 Tokyo, (JP)</p> <p>(72) 発明者; および (75) 発明者/出願人 (米国についてのみ) 稲葉隆之(INABA, Takashi)(JP/JP) 葛屋徹道(KAYA, Tetsudo)(JP/JP) 岩村浩幸(IWAMURA, Hiroyuki)(JP/JP) 〒569-11 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka, (JP)</p> <p>(74) 代理人 弁理士 高島 一(TAKASHIMA, Hajime) 〒541 大阪府大阪市中央区平野町三丁目3番9号 (湯木ビル) Osaka, (JP)</p>		<p>(81) 指定国 AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ARIPO特許 (KE, LS, MW, SD, SZ, UG), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), 欧州特許 (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI特許 (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>添付公開書類 国際調査報告書 請求の範囲の補正の期限前であり、補正書受領の際には再公開される。</p>
<p>(54)Title: NOVEL COMPOUNDS AND PHARMACEUTICAL USE THEREOF</p>		
<p>(54)発明の名称 新規化合物およびその医薬用途</p>		
<div style="text-align: center;"> <p style="text-align: center;">(I)</p> </div>		
<p>(57) Abstract Compounds represented by general formula (I) and pharmaceutically acceptable salts thereof; wherein each symbol is as defined in the specification. These compounds and salts act selectively on cannabinoid receptors, especially peripheral receptors, are reduced in the side effects against the central nervous system, and are excellent in immunomodulatory, anti-inflammatory and antiallergic activities and a nephritis curing effect, thus being useful as agonists and antagonists of cannabinoid receptors (especially peripheral cannabinoid receptors), immunomodulator, remedies for autoimmune diseases, anti-inflammatory, antiallergic, and nephritis remedy.</p>		

SPECIFICATION

NOVEL COMPOUND AND PHARMACEUTICAL USE THEREOF

TECHNICAL FIELD

The present invention relates to a novel compound which selectively acts on a cannabinoid receptor, particularly a peripheral receptor, and pharmaceutical use thereof. More particularly, the present invention relates to a novel compound that causes less central side effects and which exhibits immunoregulating action, antiinflammatory action, antiallergic action and nephritis therapy effect, and to pharmaceutical use thereof.

BACKGROUND ART

There have been heretofore known, as an indian hemp ingredient, a series of compounds called cannabinoid, consisting of C, H and O. Of these, tetrahydrocannabinol (THC) is considered to be the hallucinogen, and the main ingredient contained in hemp is known to be Δ^9 -THC. The Δ^9 -THC has been observed to cause pharmacological actions such as ataxia, increase in irritability, suppression of emesis, analgetic action, body temperature fall, suppression of respiration, induction of catalepsy, vasodilation, immunosuppressive action and the like.

The mechanism of these pharmacological actions is considered to mainly concern central nervous system (Devane et al., Mol Pharmacol. 1988, 34, 605-613; Hollister et al., Pharmacol. Rev., 1986, 38, 1-20; Renv et al., Prog. Drug. Exp. Ther., 1991, 36, 71-114) and peripheral cells (Nye et al., J. Pharmacol. Exp. Ther., 1985, 234, 784-791; Flynn et al., Mol Pharmacol. 1992, 42, 736-742), and part of the action through the central nervous system has been reported to be applicable to the medical care.

In particular, the development of an agonist of peripheral cell receptor such as one having antiinflammatory action, antiallergic action and nephritis therapy effect in addition to its immunoregulating action by regulating immunoreaction has been expected based on the finding of a receptor on macrophage (Munnro et al., Nature, 1993, 365, 61-65).

As the agonist of the cannabinoid receptor, pyrazole derivatives (Japanese Patent Unexamined Publication No. 73014/1994, EP 656354, EP 658546), THC

derivatives (Japanese Patent Unexamined Publication No. 209377/1991), benzoxazine derivatives (US 5112820), indole derivatives (US 5081122) and fatty acid derivatives (WO94/12466) are known.

There have been documented various reports on amide derivatives. For example, Japanese Patent Unexamined Publication No. 54/1986 discloses 5-lipoxygenase inhibitors such as benzoylamino acid amide; Japanese Patent Examined Publication No. 49686/1994 discloses an intermediate compound, allyl-ethylbenzamide; Japanese Patent Unexamined Publication No. 85137/1977 discloses 2-butoxyphenyl-ethylbenzamide as a hypoglycemic; Japanese Patent Unexamined Publication No. 131846/1976 discloses 2-butoxyphenyl-ethylbenzamide benzoic acid as a hypoglycemic benzoic acid derivative; Japanese Patent Unexamined Publication No. 213877/1993 discloses N-acetyl-3,4-bis(heptyloxy)-N-(2-pyridinylmethyl)benzamide as a platelet activator inhibitor; Japanese Patent Examined Publication No. 31852/1971 discloses 1-(N)-methyl-2-(4'-butoxy-2',6'-dimethylbenzoylamino)-methyl-piperidine as a local anesthetic; Japanese Patent Unexamined Publication No. 137972/1975 discloses 4-butoxy-N-(3-pyridyl)-benzamide as an antitubercular agent; US 4743610 discloses amino-alkoxy-pyridinyl-alkyl-benzamide as a thromboxane synthesis inhibitor; and Japanese Patent Unexamined Publication No. 85963/1989 discloses alkoxy-naphthalenyl-pyridinyl-amide as a platelet activator inhibitor. However, these publications do not teach pharmacological actions based on the action mechanism via cannabinoid receptors.

It is therefore an object of the present invention to provide a novel compound which selectively acts on a cannabinoid receptor, particularly a peripheral receptor, and which is free of the above-mentioned problems, and pharmaceutical use thereof.

More particularly, an object of the present invention is to provide a novel compound which selectively acts on a cannabinoid receptor, particularly, peripheral cells, which has immunoregulating action, antiinflammatory action, antiallergic action and nephritis therapy effect, and which is associated with less effects on the central nervous system (e.g., side effects such as excitation, hallucination, ataxia, increase in irritability, body temperature fall, suppression of

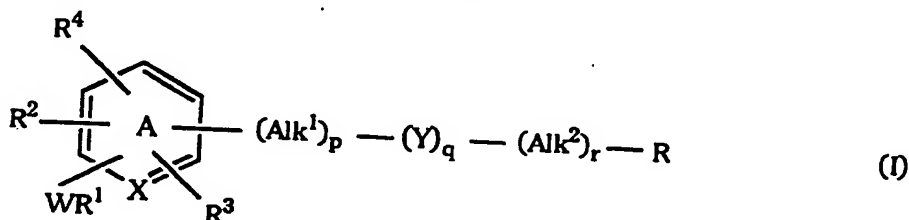
respiration, induction of catalepsy, blood pressure elevation and the like), and pharmaceutical use thereof.

DISCLOSURE OF THE INVENTION

The present inventors have made intensive studies in an attempt to achieve the above-mentioned objects and found that the novel compound of the present invention has selective affinity for a cannabinoid receptor, particularly for a peripheral cell receptor, and exhibits pharmaceutical effects in the medical conditions known to be related to a cannabinoid receptor, particularly the medical conditions (e.g., immune diseases, various inflammations, allergic diseases, nephritis and the like) known to be related to peripheral cell tissues.

Accordingly, the present invention provides the following.

- (1) A cannabinoid receptor activator or antagonist comprising, as an active ingredient, a compound of the formula (I)



wherein

X is CH or N;

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-
wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl
wherein

each group at R¹ is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R² is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroaryl-

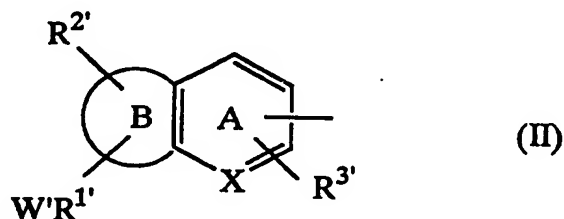
alkyl, cycloalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, or R^8 and R^9 optionally form heteroaryl together with the adjacent nitrogen atom, or $-(CH_2)_uS(O)_{u'}R^{12}$ wherein R^{12} is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxy-carbonyl, a halogen atom or nitro, said alkyl being optionally substituted by alkoxy or hydroxy;

R^4 is a hydrogen atom, or R^4 and R^2 form, together with A ring, a condensed ring of the formula (II)



wherein $WR^{1'}$, $R^{2'}$ and $R^{3'}$ are substituted at an optional position of A ring or B ring, $WR^{1'}$, $R^{2'}$ and $R^{3'}$ are each as defined above for WR^1 , R^2 and R^3 , respectively, and B ring is a benzene ring, pyridine ring or furan ring;

Alk^1 is $-CH=CH-$, $-CH_2CH_2-$ or $-C\equiv C-$;

Y is $-CONR^{10}-$, $-NR^{11}CO-$, $-COO-$, $-CH_2NR^{10}-$ or $-NHCONH-$ wherein,

R^{10} and R^{11} are the same or different and each is hydrogen atom, alkyl, alkenyl or amino-protecting group, said alkyl

being optionally substituted by heteroaryl, arylsulfinyl or alkoxy carbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene, an alkenylene, $-\text{COCH}_2-$ or $-\text{CONH}(\text{CH}_2)_v-$ wherein v is 0, 1 or 2 wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted hydroxy, carboxyl, alkoxy carbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-\text{CONR}^{13}\text{R}^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl wherein

said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, pyridyl, piperidino, carboxyl, alkoxy carbonyl, acylamino, aminocarbonyl or cyano, said cycloalkyl is optionally substituted by hydroxy, alkoxy or $=\text{O}$, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

p , q and r are each independently 0 or 1,

provided that

when $p=1$ and $q=1$, Alk^1 is $-\text{CH}=\text{CH}-$, Y is $-\text{CONR}^{10}-$, and R^3 and R^{10} in combination optionally show $-\text{NHCO}-$ to form a condensed ring with A ring,

when $p=0$ and $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R^3 and R^{10} in combination optionally show $-\text{CH}=\text{CH}-$, $-\text{CH}_2\text{CHR}^{27}-$, $-\text{CH}_2-$, $-\text{S}-$, $-\text{CHOH}-$, $-\text{CO}-$, $-\text{CH}_2\text{CO}-$, $-\text{NHCR}^{28}(\text{CH}_2)_v-$, $-\text{NHCR}^{29}\text{R}^{30}-$ or $-\text{N}=\text{CR}^{31}-$ to form a condensed ring with A ring

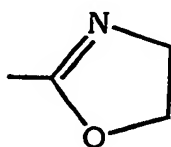
wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl,

R^{31} is alkyl or hydrogen atom and v' is 0 or 1,

when $r=0$ and $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R and R^{10} optionally form heteroaryl together with the adjacent nitrogen atom, and

when $p=q=r=0$, R is a group of the formula (i)

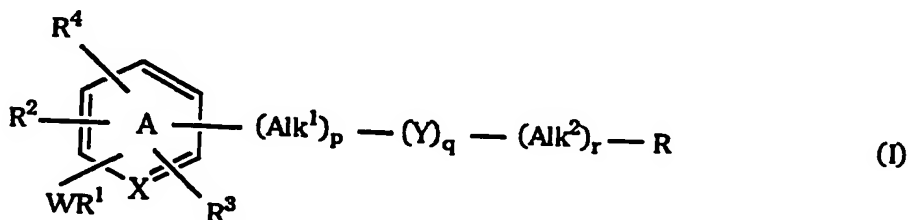


(i)

wherein said group is optionally substituted by alkyl optionally substituted by hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkyl-amino, aralkyloxy or pyridyl;

[hereinafter also referred to as Compound (I)], and a pharmaceutically acceptable salt thereof.

(2) A cannabinoid receptor activator or antagonist of (1) above, comprising, as an active ingredient, a compound of the formula (I)



(I)

wherein

X is CH or N ;

W is $-\text{O}-$, $-\text{S}(\text{O})_t-$, $-\text{CR}^5\text{R}^6-$, $-\text{NR}^7-$, $-\text{NR}^7\text{CO}-$ or $-\text{CONR}^7-$.

wherein

R^5 and R^6 are the same or different and each is hydrogen atom or alkyl, R^7 is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^1 is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl

wherein

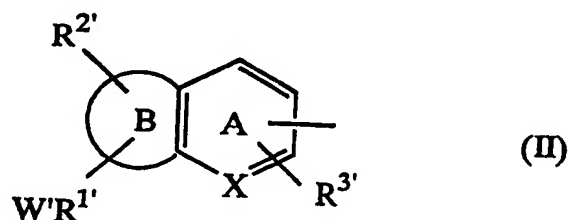
each group at R^1 is optionally substituted by alkyl, alkylamino or hydroxy;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl or acyl, or $-(CH_2)_uS(O)_{u'}R^{12}$ wherein R^{12} is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2 wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino or hydroxy;

R^3 is a hydrogen atom, an alkoxy, an alkyl, an alkoxycarbonyl, a halogen atom or nitro, said alkyl being optionally substituted by hydroxy;

R^4 is a hydrogen atom, or R^4 and R^2 form, together with A ring, a condensed ring of the formula (II)



wherein $WR^{1'}$, $R^{2'}$ and $R^{3'}$ are substituted at an optional position of A ring or B ring, $WR^{1'}$, $R^{2'}$ and $R^{3'}$ are each as defined above for WR^1 , R^2 and R^3 , respectively, and B ring is a benzene ring or furan ring;

Alk^1 is $-CH=CH-$ or $-CH_2CH_2-$;

Y is $-CONR^{10}-$, $-NR^{11}CO-$, $-COO-$, $-CH_2NR^{10}-$ or $-NHCONH-$ wherein

R^{10} and R^{11} are the same or different and each is hydrogen atom, alkyl, alkenyl or amino-protecting group, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxycarbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk² is an alkylene, an alkenylene, -COCH₂- or -CONH(CH₂)_v- wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk² are each optionally substituted hydroxy, carboxyl, alkoxy, carbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or -CONR¹³R¹⁴ wherein R¹³ and R¹⁴ are the same or different and each is hydrogen atom or alkyl;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl, hydroxy, alkoxy, alkenyloxy, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, piperidino, carboxyl, acylamino, aminocarbonyl or cyano, said cycloalkyl is optionally substituted by hydroxy or =O, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy; and

p, q and r are each independently 0 or 1,

provided that

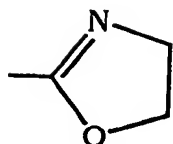
when p=0 and q=1, Y is -CONR¹⁰- or -CH₂NR¹⁰-, and R⁹ and R¹⁰ in combination optionally show -CH=CH-, -CH₂CHR²⁷-, -CH₂-, -S-, -CHOH-, -CO-, -CH₂CO-, -NHCR²⁸(CH₂)_v-, -NHCR²⁹R³⁰- or -N=CR³¹- to form a condensed ring with A ring wherein

R²⁷ is hydrogen atom or hydroxy, R²⁸ is oxygen atom or sulfur atom, R²⁹ and R³⁰ are the same or different and each is alkyl,

R³¹ is alkyl or hydrogen atom and v' is 0 or 1,

when r=0 and q=1, Y is -CONR¹⁰- or -CH₂NR¹⁰-, and R and R¹⁰ optionally form heteroaryl together with the adjacent nitrogen atom, and

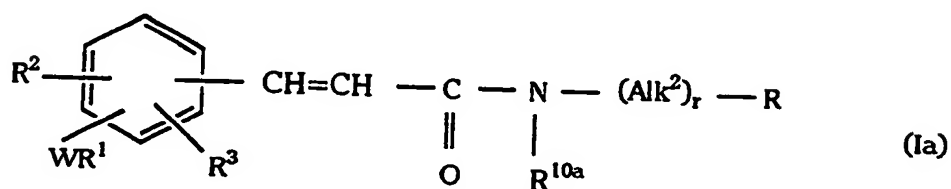
when p=q=r=0, R is a group of the formula (i)



(i)

wherein said group is optionally substituted by alkyl or pyridyl;
and a pharmaceutically acceptable salt thereof.

(3) A compound of the formula (Ia)



(Ia)

wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;
R¹ is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl
wherein

each group at R¹ is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R² is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, or R⁸ and R⁹ optionally form heteroaryl together with the adjacent nitrogen atom, or -(CH₂)_n-S(O)_n-R¹² wherein R¹² is hydrogen atom, alkyl, alkenyl

or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy-carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxy-carbonyl or a halogen atom, said alkyl being optionally substituted by alkoxy or hydroxy;

R^{10a} is a hydrogen atom, an alkyl, an alkenyl or an amino-protecting group, said alkyl being optionally substituted by heteroaryl or arylsulfinyl;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted by hydroxy, carboxyl, alkoxy-carbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

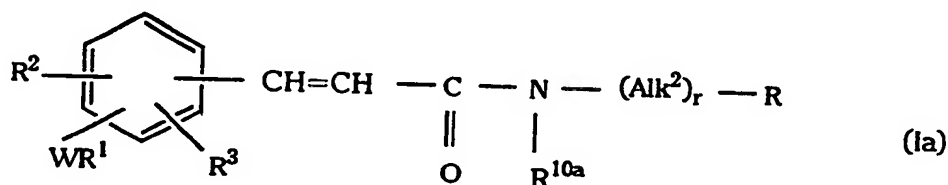
said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, cyano, aralkyloxy or pyridyl, said cycloalkyl is optionally substituted by hydroxy, alkoxy or $=O$, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

provided that when $r=0$, R and R^{10a} optionally form heteroaryl together with the adjacent nitrogen atom;

[hereinafter also referred to as Compound (Ia)] and a pharmaceutically acceptable salt thereof.

(4) A compound of (3) above, which is represented by the formula (Ia)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶- or -NR⁷-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl wherein

each group at R¹ is optionally substituted by alkyl or alkylamino;

R² is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom or alkyl, or -(CH₂)_uS(O)_{u'}R¹² wherein R¹² is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2 wherein

each group at said R² except hydrogen atom is optionally substituted by alkyl or alkylamino;

R³ is a hydrogen atom or an alkoxy;

R^{10a} is a hydrogen atom or an alkyl, said alkyl being optionally substituted by heteroaryl;

Alk² is an alkylene

wherein

said alkylene is optionally substituted by alkoxycarbonyl, alkyl optionally substituted by hydroxy, or -CONR¹³R¹⁴ wherein R¹³ and R¹⁴

are the same or different and each is hydrogen atom or alkyl;
 R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed
 cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl,
 hydroxy, alkoxy, alkenyloxy, acyloxy, halogen atom, nitro, amino,
 sulfonamide, alkylamino or cyano, said cycloalkyl is optionally
 substituted by hydroxy, and said benzene-condensed cycloalkyl is
 optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

provided that when $r=0$, R and R^{10a} optionally form morpholino or
 imidazolyl together with the adjacent nitrogen atom;

and a pharmaceutically acceptable salt thereof.

(5) The compound of (4), wherein R^9 is hydrogen atom, R^2 is $-OR^{15}$,
 $-NR^8R^9$ or $-(CH_2)_nS(O)_mR^{12}$, and R^2 is substituted at the para position on the
 benzene ring and $-WR^1$ is substituted at the meta position on the benzene ring,
 both relative to the binding site of $-CH=CH-CO-NR^{10a}-(Alk^2)_r-R$ on the benzene ring,
 and a pharmaceutically acceptable salt thereof.

(6) The compound of (5), wherein R^1 is alkyl having 4 to 6 carbon atoms, and a
 pharmaceutically acceptable salt thereof.

(7) The compound of (6), wherein Alk^2 is ethylene, and a pharmaceutically
 acceptable salt thereof.

(8) The compound of (4), wherein, when $r=0$, R and R^{10a} form morpholino together
 with the adjacent nitrogen atom, and a pharmaceutically acceptable salt thereof.

(9) The compound of (7), which is selected from the group consisting of
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-
 acrylamide,

3-(4-ethoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]-
 acrylamide,

3-(3,4-dipentyloxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-butyloxyphenyl)-
 acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-hexyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-heptyloxyphenyl)-acrylamide,

(E)-N-[2-(3-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(2-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxycyclohexyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-N-methyl-3-(4-methoxy-3-pentyloxyphenyl)acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-isopentyloxy-4-methoxyphenyl)-acrylamide,

3-[3-(2-ethylbutyloxy)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)acrylamide,

3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(3,4-dihydroxyphenyl)ethyl]-3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]acrylamide,

3-(3-hexyl-4-methoxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-(4-amino-3-pentyloxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-(4-amino-3-pentyloxyphenyl)-N-[2-(4-nitrophenyl)ethyl]acrylamide,

3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-pentyloxyphenyl)ethyl]-acrylamide,

(E)-N-[2-(4-methoxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-(2-morpholinoethyl)acrylamide,

(E)-N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-

acrylamide,
 2-[2-{3-(3-pentyloxy-4-methoxyphenyl)acryloylamino}ethyl]pyridine-N-oxide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-
 acrylamide,
 3-[3-(N',N'-dipentylamino)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxy-
 phenyl)ethyl]acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentylamino-4-pentyloxyphenyl)-
 acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-[3-(N'-methyl-N'-pentylamino)-4-
 methoxyphenyl]acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-pentyloxy-3-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)acryl-
 amide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentyloxy-4-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentyloxy-4-methylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(imidazol-4-yl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-
 acrylamide,
 (E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-
 acrylamide,
 (E)-N-[2-(imidazol-4-yl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-
 acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methylamino-3-pentyloxy-
 phenyl)acrylamide,

(E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-acrylamide,

(E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methylamino-3-pentyloxyphenyl)-acrylamide,

3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-thiophen-2-yl)ethyl]-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-[(N'-methyl-N'-pentylamino)-4-pentyloxyphenyl]acrylamide,

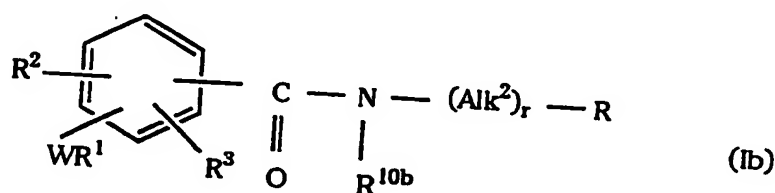
(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-pentylamino-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-cyanophenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide and

(E)-N-[2-(4-carbamoylphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

and a pharmaceutically acceptable salt thereof.

(10) A compound of the formula (Ib)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl wherein

each group at R¹ is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio,

mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, or R^8 and R^9 optionally form heteroaryl together with the adjacent nitrogen atom, or $-(CH_2)_uS(O)_uR^{12}$ wherein R^{12} is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxy-carbonyl, nitro or a halogen atom, said alkyl being optionally substituted by alkoxy or hydroxy;

R^{10a} is a hydrogen atom, an alkyl, an alkenyl or an amino-protecting group, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxycarbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted by hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed

cycloalkyl

wherein

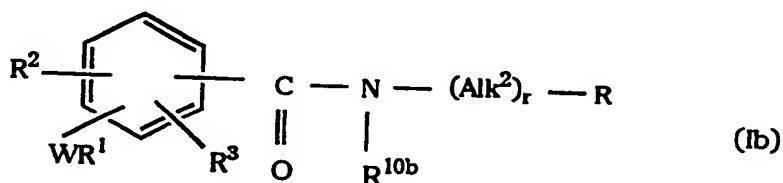
said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy or pyridyl, said cycloalkyl is optionally substituted by hydroxy, alkoxy or =O, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

provided that when r=0, R and R^{10b} optionally form heteroaryl together with the adjacent nitrogen atom;

[hereinafter also referred to as Compound (Ib)], and a pharmaceutically acceptable salt thereof.

(11) A compound of (10) above, which is represented by the formula (Ib)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷- or -NR⁷CO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl wherein

each group at R¹ is optionally substituted by alkyl, alkylamino or hydroxy;

R² is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom, alkyl or

acyl, or $-(CH_2)_u-S(O)_uR^{12}$ wherein R^{12} is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino or hydroxy;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a nitro or a halogen atom, said alkyl being optionally substituted by hydroxy;

R^{10a} is a hydrogen atom, an alkyl or an alkenyl, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxycarbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene or an alkenylene wherein

said alkylene and alkenylene are each optionally substituted by hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl, hydroxy, alkenyloxy, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino or aralkyloxy, said cycloalkyl is optionally substituted by hydroxy, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy; and

r is 0 or 1,

provided that when $r=0$, R and R^{10a} optionally form morpholino or imidazolyl together with the adjacent nitrogen atom;

and a pharmaceutically acceptable salt thereof.

(12) The compound of (11), wherein R^3 is hydrogen atom, R^2 is $-OR^{15}$, $-NR^8R^9$ or $-(CH_2)_u-S(O)_uR^{12}$, and R^2 is substituted at the para-position on the benzene ring and $-WR^1$ is substituted at the meta-position on the benzene ring, both relative to the binding site of

-CO-NR^{10b}-(Alk²)-R on the benzene ring, and a pharmaceutically acceptable salt thereof.

(13) The compound of (12), wherein R¹ is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(14) The compound of (13), wherein Alk² is ethylene, and a pharmaceutically acceptable salt thereof.

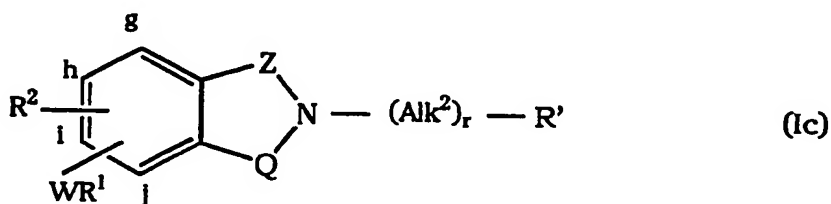
(15) The compound of (14), which is selected from the group consisting of

N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 4-ethoxy-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,
 3,4-dipentyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 4-dimethylamino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentylamino-4-methoxybenzamide,
 3-butyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-hexyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-heptyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(3-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(2-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxycyclohexyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-N-methyl-4-methoxy-3-pentyloxybenzamide,
 3-isopentyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-(2-ethylbutyloxy)-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-4-hydroxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxy-N-methyl-3-pentyloxybenzamide,
 3-(1,1-dimethylheptane)-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(1,1-dimethylheptane)-4-methoxybenzamide,
 3-(1,1-dimethylheptane)-N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-4-methoxybenzamide,
 3-(1,1-dimethylheptane)-N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxybenzamide,
 N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(1,1-dimethylheptane)-4-hydroxybenzamide,
 3-hexyl-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,

N-[2-(4-aminophenyl)ethyl]-3,4-dipentyloxybenzamide,
 3,4-dihexyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 4-methoxy-N-[2-(4-pentyloxyphenyl)ethyl]-3-pentyloxybenzamide,
 4-methoxy-N-(2-morpholinoethyl)-3-pentyloxybenzamide,
 4-methoxy-N-[2-(4-propen-2-yloxyphenyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-N-[2-(phenylsulfinyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(3,4-dihydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-acetoxyphenyl)ethyl]-4-methoxy-3-pentyloxy-N-(E)-phenylthiovinylbenzamide,
 N-[2-(4-acetoxyphenyl)ethyl]-N-ethyl-4-methoxy-3-pentyloxybenzamide,
 4-[2-{N-(4-methoxy-3-pentyloxybenzoyl)amino}ethyl]pyridine-N-oxide,
 3-[2-{N-(4-methoxy-3-pentyloxybenzoyl)amino}ethyl]pyridine-N-oxide,
 3-dipentylamino-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-isohexyl-4-methoxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-(N'-methyl-N'-pentylamino)-benzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentylamino-4-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-pentylamino-3-pentyloxybenzamide,
 3,4-dipentyloxy-N-[2-(4-sulfamoylphenyl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(imidazol-4-yl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(4-nitrophenyl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(4-fluorophenyl)ethyl]benzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxy-4-propen-2-ylbenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-propyloxy-3-pentyloxybenzamide,
 3,4-dibutyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 3,4-diheptyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methylamino-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3,4-dipentylaminobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-(N'-methyl-N'-pentylamino)-4-pentyloxybenzamide,
 4-amino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,

N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-pentyloxy-3-pentylthiobenzamide,
 3,4-dipentyloxy-N-[2-(2-thienyl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(5-hydroxyindol-3-yl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(4-methylaminophenyl)ethyl]benzamide,
 N-[2-(4-dimethylaminophenyl)ethyl]-3,4-dipentyloxybenzamide,
 4-butyrylamino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-formylamino-3-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methylthio-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxy-4-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-(4-hydroxybutyloxy)-4-methoxybenzamide,
 N-[2-(4-aminophenyl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentylthiobenzamide,
 N-[2-(imidazol-4-yl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 N-[2-(4-aminophenyl)ethyl]-4-pentyloxy-3-pentylthiobenzamide,
 N-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-3-pentylthiobenzamide and
 N-[2-(imidazol-4-yl)ethyl]-4-pentyloxy-3-pentylthiobenzamide,
 and a pharmaceutically acceptable salt thereof.

(16) A compound of the formula (Ic)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl

wherein

each group at R^1 is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, or R^8 and R^9 optionally form heteroaryl together with the adjacent nitrogen atom, or $-(CH_2)_uS(O)_uR^{12}$ wherein R^{12} is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

Z is $-CH_2-$ or $-CO-$;

Q is $-CH=CH-$, $-CH_2CHR^{27}-$, $-CH_2-$, $-S-$, $-CHOH-$, $-CO-$, $-CH_2CO-$, $-NHCR^{28}(CH_2)_v-$, $-NHCR^{29}R^{30}-$ or $-N=CR^{31}-$

wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl,

R^{31} is alkyl or hydrogen atom and v is 0 or 1;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted by hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and

each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R' is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

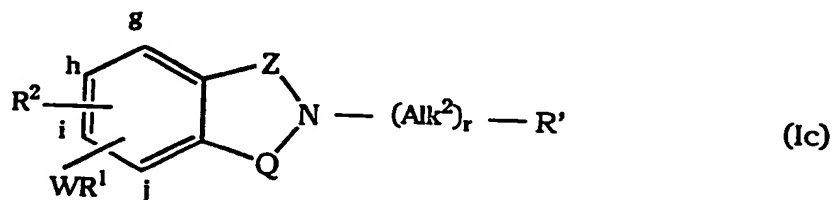
wherein

said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, acylamino, piperidino or pyridyl, said cycloalkyl is optionally substituted by hydroxy, alkoxy or =O, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

[hereinafter also referred to as Compound (Ic)], and a pharmaceutically acceptable salt thereof.

(17) A compound of (16) above, which is represented by the formula (Ic)



wherein

W is $-O-$, $-S(O)_t-$, $-CR^5R^6-$, $-NR^7-$ or $-NR^7CO-$

wherein

R^5 and R^6 are the same or different and each is hydrogen atom or alkyl, R^7 is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^1 is an alkyl;

R^2 is a hydrogen atom, an alkyl or $-OR^{15}$ wherein R^{15} is hydrogen atom or alkyl;

Z is $-CH_2-$ or $-CO-$;

Q is $-CH=CH-$, $-CH_2CHR^{27}-$, $-CH_2-$, $-S-$, $-CHOH-$, $-CO-$, $-CH_2CO-$,

$-\text{NHCR}^{28}(\text{CH}_2)_v-$, $-\text{NHCR}^{29}\text{R}^{30}-$ or $-\text{N}=\text{CR}^{31}-$

wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl, R^{31} is alkyl or hydrogen atom and v is 0 or 1;

Alk^2 is an alkylene, $-\text{COCH}_2-$ or $-\text{CONH}(\text{CH}_2)_v-$ wherein v is 0, 1 or 2;

R' is an aryl, a heteroaryl or a cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl, hydroxy, acyloxy, nitro, amino, alkylamino, aralkyloxy, acylamino or piperidino, and said cycloalkyl is optionally substituted by $=\text{O}$;

r is 0 or 1,

and a pharmaceutically acceptable salt thereof.

(18) The compound of (17), wherein Z is $-\text{CO}-$ and Q is $-\text{CH}_2-$, and a pharmaceutically acceptable salt thereof.

(19) The compound of (18), wherein R^2 is $-\text{OR}^{15}$, W is $-\text{O}-$, $-\text{NR}^7-$ or $-\text{NR}^7\text{CO}-$, R^2 is substituted at the i -position on the benzene ring, and $-\text{WR}^1$ is substituted at the j -position on the benzene ring, and a pharmaceutically acceptable salt thereof.

(20) The compound of (19), wherein R^1 is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(21) The compound of (20), which is selected from the group consisting of

2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
2-[2-(4-benzyloxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,

5-methoxy-2-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one,
2-[2-(4-methylphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,

4,5-dipentyloxy-2-[2-(imidazol-4-yl)ethyl]-2,3-dihydroisoindol-1-one,

2-[2-(4-benzyloxyphenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,

4,5-dipentyloxy-2-[2-(4-nitrophenyl)ethyl]-2,3-dihydroisoindol-1-one,

2-[2-(4-aminophenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,

4,5-dipentyloxy-2-[2-(4-hydroxyphenyl)ethyl]-2,3-dihydroisoindol-1-one,

4,5-dipentyloxy-2-[2-(4-methylaminophenyl)ethyl]-2,3-dihydroisoindol-1-one,

2-[2-(4-dimethylaminophenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-aminophenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentylamino-2,3-dihydroisoindol-1-one,

5-methoxy-4-pentyloxy-2-[2-(4-pyridine)ethyl]-2,3-dihydroisoindol-1-one,
 2-[2-(4-dimethylaminophenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one and

5-methoxy-2-[2-(4-methylaminophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one,

and a pharmaceutically acceptable salt thereof.

(22) The compound of (17), wherein Z is -CO- and Q is -CH=CH-, and a pharmaceutically acceptable salt thereof.

(23) The compound of (22), wherein R² is -OR²⁵, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, and a pharmaceutically acceptable salt thereof.

(24) The compound of (23), wherein R¹ is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(25) The compound of (24), which is selected from the group consisting of

2-[2-(4-benzyloxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-pyridyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 4-[2-(6-methoxy-1-oxo-5-pentyloxy-1H-isoquinolin-2-yl)ethyl]phenyl acetate,
 6-methoxy-2-[2-(4-nitrophenyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-methylphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 6-methoxy-5-pentyloxy-2-(2-phenylethyl)-2H-isoquinolin-1-one,
 2-[2-(4-acetylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 5,6-dipentyloxy-2-[2-(4-hydroxyphenyl)ethyl]-2H-isoquinolin-1-one,
 2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one
 hydrochloride,
 2-[2-(4-dimethylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,

2-[2-(4-methylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,

6-methoxy-2-[2-(4-piperidinophenyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one
and

6-methoxy-2-[2-(4-pyridyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one
hydrochloride,

and a pharmaceutically acceptable salt thereof.

(26) The compound of (17), wherein Z is -CO- and Q is -CH₂CHR²⁷- wherein R²⁷ is hydrogen atom, and a pharmaceutically acceptable salt thereof.

(27) The compound of (26), wherein R² is -OR¹⁵, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, and a pharmaceutically acceptable salt thereof.

(28) The compound of (27), wherein R¹ is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(29) The compound of (28), which is selected from the group consisting of

6-methoxy-2-[2-(4-oxocyclohexyl)ethyl]-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

4-[2-(6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)-ethyl]phenyl acetate,

2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-(2-phenylethyl)-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-acetylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

6-hydroxy-2-[2-(4-hydroxyphenyl)ethyl]-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-methylphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

6-methoxy-5-pentyloxy-2-[2-(4-pyridyl)ethyl]-3,4-dihydro-2H-isoquinolin-1-one,

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-

(4-aminophenyl)amide,

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-[(4-aminophenyl)methyl]amide and

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-(4-nitrophenyl)amide,

and a pharmaceutically acceptable salt thereof.

(30) The compound of (17), wherein Z is -CO- and Q is -NHCR^{2a}(CH₂)_v- wherein R^{2a} is oxygen atom and v' is 0, and a pharmaceutically acceptable salt thereof.

(31) The compound of (30), wherein R² is -OR^{1a}, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, and a pharmaceutically acceptable salt thereof.

(32) The compound of (31), wherein R¹ is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(33) The compound of (32), which is selected from the group consisting of 7-methoxy-3-[2-(4-nitrophenyl)ethyl]-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

7-methoxy-3-[2-(4-pyridyl)ethyl]-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

3-[2-(4-aminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

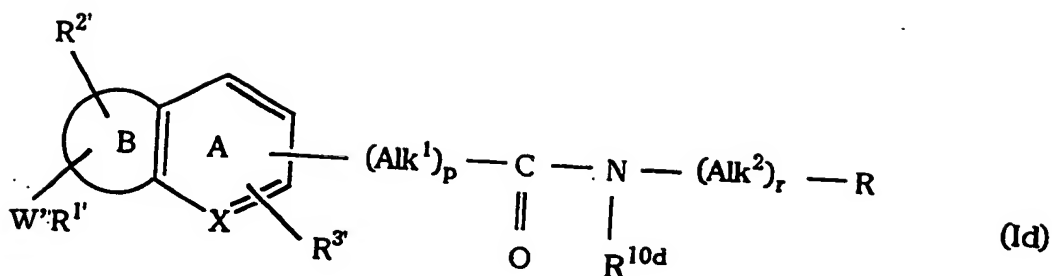
3-[2-(4-hydroxyphenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

3-[2-(4-methylaminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione and

3-[2-(4-dimethylaminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

and a pharmaceutically acceptable salt thereof.

(34) A compound of the formula (Id)



wherein

X is CH or N;

W' is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-
wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^{1'} is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl
wherein

each group at R^{1'} is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^{2'} is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, or R⁸ and R⁹ optionally form heteroaryl together with the adjacent nitrogen atom, or -(CH₂)_u-S(O)_{u'}R¹² wherein R¹² is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2
wherein

each group at said R^{2'} except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio,

alkylsulfinyl or alkylsulfonyl;

$R^{3'}$ is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxy-carbonyl or a halogen atom, said alkyl being optionally substituted by alkoxy or hydroxy;

$WR^{1'}$, $R^{2'}$ and $R^{3'}$ are substituted at an optional position of A ring or B ring, and B ring is a benzene ring, pyridine ring or furan ring;

Alk^1 is $-CH=CH-$, $-CH_2CH_2-$ or $-C\equiv C-$;

R^{10a} is a hydrogen atom, an alkyl, an alkenyl or an amino-protecting group, said alkyl being optionally substituted by heteroaryl or arylsulfinyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted by hydroxy, carboxyl, alkoxy, carbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

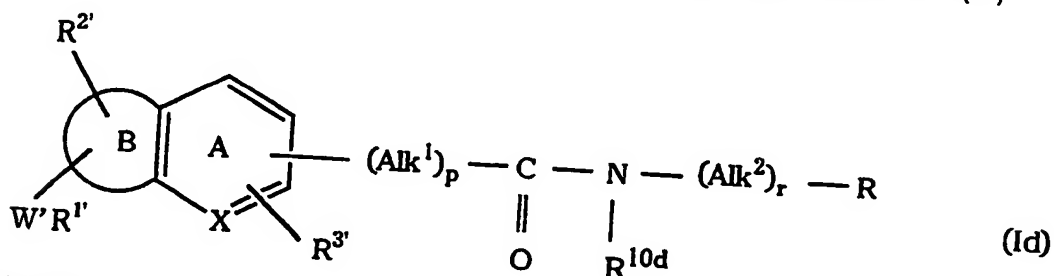
said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy or pyridyl, said cycloalkyl is optionally substituted by hydroxy, alkoxy or $=O$, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

p and r are each independently 0 or 1,

provided that when $r=0$, R and R^{10a} optionally form heteroaryl

together with the adjacent nitrogen atom;
[hereinafter also referred to as Compound (Id)] and a pharmaceutically acceptable salt thereof.

(35) A compound of (34) above, which is represented by the formula (Id)



wherein

X is CH or N;

W' is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷- or -NR⁷CO-
wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl;

R² is a hydrogen atom, an alkyl or -OR¹⁵ wherein R¹⁵ is hydrogen atom or alkyl;

R³ is a hydrogen atom or a halogen atom;

W'R¹, R² and R³ are substituted at an optional position of A ring or B ring, and B ring is a benzene ring or furan ring;

Alk¹ is -CH=CH- or -CH₂CH₂-;

R^{10d} is a hydrogen atom;

Alk² is an alkylene;

R is an aryl or a heteroaryl

wherein

said aryl and heteroaryl are each optionally substituted by hydroxy, nitro or amino; and

p and r are each independently 0 or 1,

and a pharmaceutically acceptable salt thereof.

(36) The compound of (35), wherein X is N, and a pharmaceutically acceptable salt

thereof.

(37) The compound of (36), wherein $R^{3'}$ is hydrogen atom, $R^{2'}$ is $-OR^{15}$, W is $-O-$, and a pharmaceutically acceptable salt thereof.

(38) The compound of (37), wherein $R^{1'}$ is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(39) The compound of (38), which is selected from the group consisting of

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-pyridyl)-ethyl]amide,

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-hydroxy-phenyl)ethyl]amide,

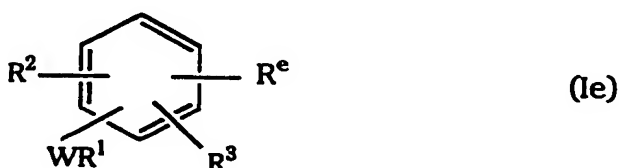
7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-aminophenyl)-ethyl]amide,

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-nitrophenyl)-ethyl]amide and

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(imidazol-4-yl)ethyl]amide,

and a pharmaceutically acceptable salt thereof.

(40) A compound of the formula (Ie)



wherein

W is $-O-$, $-S(O)_t-$, $-CR^5R^6-$, $-NR^7-$, $-NR^7CO-$, $-CONR^7-$, $-COO-$ or $-OCO-$ wherein

R^5 and R^6 are the same or different and each is hydrogen atom or alkyl, R^7 is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^1 is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl wherein

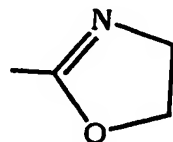
each group at R^1 is optionally substituted by alkyl, alkylamino,

amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;
 R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroaryl-alkyl, cycloalkyl or cycloalkylalkyl, or R^8 and R^9 optionally form heteroaryl together with the adjacent nitrogen atom, or $-(CH_2)_uS(O)_uR^{12}$ wherein R^{12} is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2
 wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxycarbonyl or a halogen atom, said alkyl being optionally substituted by alkoxy or hydroxy; and

R^6 is a group of the formula (i)

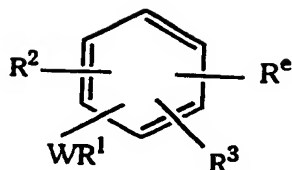


(i)

wherein said group is optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkyl-amino, aralkyloxy or pyridyl,

[hereinafter also referred to as Compound (Ie)], and a pharmaceutically acceptable salt thereof.

(41) A compound of (40) above, which is represented by the formula (Ie)



(1e)

wherein

W is $-O-$ or $-S(O)_t-$

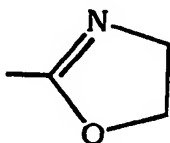
wherein t is 0, 1 or 2;

R^1 is an alkyl;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom or alkyl, or $-(CH_2)_u-S(O)_v-R^{12}$ wherein R^{12} is alkyl, u is 0, 1 or 2 and v is 0, 1 or 2;

R^3 is a hydrogen atom, an alkoxy, an alkyl, an alkoxy carbonyl or a halogen atom, said alkyl being optionally substituted by hydroxy; and

R^4 is a group of the formula (i)



(i)

wherein said group is optionally substituted by alkyl or pyridyl, and a pharmaceutically acceptable salt thereof.

(42) The compound of (41), wherein R^2 is $-OR^{15}$, or $-(CH_2)_u-S(O)_v-R^{12}$, R^2 is substituted at the para-position on the benzene ring, and $-WR^1$ is substituted at the meta-position on the benzene ring, both relative to the binding site of R^4 on the benzene ring, and a pharmaceutically acceptable salt thereof.

(43) The compound of (42), wherein R^1 is alkyl having 4 to 6 carbon atoms, and a pharmaceutically acceptable salt thereof.

(44) The compound of (43), which is selected from the group consisting of

- 2-(4-methoxy-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole,
- 2-(4-methoxy-3-pentylthiophenyl)-4,4-dimethyl-4,5-dihydrooxazole,
- 2-(3,4-dipentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole,
- 2-(4-methylthio-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole,
- 2-(3-pentyloxy-4-pentylthiophenyl)-4,4-dimethyl-4,5-dihydrooxazole,

2-(4-pentyloxy-3-pentylthiophenyl)-4,4-dimethyl-4,5-dihydrooxazole and 2-(4-methoxy-3-pentyloxyphenyl)-5-(2-pyridyl)-4,5-dihydrooxazole, and a pharmaceutically acceptable salt thereof.

(45) A pharmaceutical composition comprising, as an active ingredient, any one of the compounds of (3) to (44), or a pharmaceutically acceptable salt thereof.

(46) A cannabinoid receptor activator or antagonist of (1) or (2), wherein the cannabinoid receptor is a peripheral cannabinoid receptor.

(47) The cannabinoid receptor activator or antagonist of any one of (1), (2) and (46), which is an immunoregulator.

(48) The cannabinoid receptor activator or antagonist of any one of (1), (2) and (46), which is a therapeutic agent for autoimmune diseases.

(49) The cannabinoid receptor activator or antagonist of any one of (1), (2) and (46), which is an antiinflammatory agent.

(50) The cannabinoid receptor activator or antagonist of any one of (1), (2) and (46), which is an antiallergic agent.

(51) The cannabinoid receptor activator or antagonist of any one of (1), (2) and (46), which is a therapeutic agent for nephritis.

The groups used in the present specification are explained in the following.

Alkyl may be linear or branched and exemplified by methyl, ethyl, propyl, isopropyl, butyl, isobutyl, s-butyl, t-butyl, pentyl, isopentyl, neopentyl, t-pentyl, hexyl, isohexyl, neohexyl, heptyl and the like. The alkyl at R^2 , R^3 , R^3' , R^7 , R^8 , R^9 , R^{12} , R^{15} , R^{29} , R^{30} and R^{31} preferably has 1 to 7 carbon atoms; that at R^{29} , R^{30} and R^{31} more preferably has 1 or 2 carbon atoms; that at R^2 and $R^{2'}$ more preferably has 1 or 5 carbon atoms; that at R^5 , R^6 , R^{10} , R^{10a} , R^{10b} , R^{10d} , R^{11} , R^{13} and R^{14} preferably has 1 to 4 carbon atoms; and that at R^1 and $R^{1'}$ preferably has 4 to 6 carbon atoms.

The alkenyl may be linear or branched and is exemplified by vinyl, allyl, crotyl, 2-pentenyl, 3-pentenyl, 2-hexenyl, 3-hexenyl, heptenyl and the like. The alkenyl at R^8 , R^9 , R^{12} and R^{15} preferably has 2 to 7 carbon atoms; that at R^{10} , R^{10a} , R^{10b} , R^{10d} and R^{11} preferably has 2 to 4 carbon atoms; and that at R^1 and $R^{1'}$ preferably has 4 to 7 carbon atoms.

The alkynyl may be linear or branched and is exemplified by ethynyl,

propynyl, butynyl, 2-pentynyl, 3-pentynyl, 2-hexynyl, 3-hexynyl, heptynyl and the like. The alkynyl at R^8 , R^9 , R^{12} and R^{15} preferably has 2 to 7 carbon atoms; and that at R^1 and R^{13} preferably has 4 to 7 carbon atoms.

The alkylene at Alk^2 may be linear or branched and preferably has 1 to 4 carbon atoms. Examples thereof include methylene, ethylene, trimethylene, tetramethylene and the like, with preference given to that having 2 carbon atoms.

The alkenylene at Alk^2 may be linear or branched and preferably has 2 to 4 carbon atoms. Examples thereof include vinylene, propenylene, butenylene and the like.

The alkoxy at R^8 and $R^{3'}$ may be linear or branched and preferably has 1 to 7 carbon atoms. Examples thereof include methoxy, ethoxy, propoxy, isopropoxy, butoxy, isobutoxy, s-butoxy, t-butoxy, pentyloxy, isopentyloxy, neopentyloxy, hexyloxy, heptyloxy and the like.

The alkoxycarbonyl at R^8 and $R^{3'}$ preferably has 2 to 5 carbon atoms, and is exemplified by the above-mentioned alkoxy having 1 to 4 carbon atoms plus carbonyl. Specific examples thereof include methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and the like.

The acyl at R^8 and R^9 preferably has 1 to 5 carbon atoms and is exemplified by formyl, acetyl, propionyl, butyryl, isobutyryl, valeryl, isovaleryl, pivaloyl and the like.

The cycloalkyl is exemplified by cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like. The cycloalkyl at R^1 , $R^{1'}$, R^8 , R^9 and R^{15} preferably has 3 to 6 carbon atoms; and that at R preferably has 3 to 7 carbon atoms, and more preferably has 6 carbon atoms.

With regard to the cycloalkylalkyl at R^1 , $R^{1'}$, R^8 , R^9 and R^{15} , the cycloalkyl moiety is that exemplified above which has 3 to 6 carbon atoms, and the alkyl moiety is that exemplified above which has 1 to 4 carbon atoms. Specific examples include cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, cyclopropylethyl, cyclopropylpropyl, cyclopropylbutyl and the like.

The aryl at R^1 , $R^{1'}$, R^8 , R^9 , R^{15} and R is exemplified by phenyl, naphthyl, biphenyl and the like, with preference given to phenyl.

With regard to the arylalkyl at R^1 , $R^{1'}$, R^8 , R^9 and R^{15} , the aryl moiety is that exemplified above and the alkyl moiety is that exemplified above which has 1 to 4 carbon atoms. Specific examples include benzyl, phenethyl, phenylpropyl, phenylbutyl, naphthylmethyl, biphenylmethyl and the like, with preference given to benzyl.

The heteroaryl at R^1 , $R^{1'}$, R^8 , R^9 , R^{15} and R may be saturated with hydrogen atom, and is exemplified by pyrimidyl, pirazinyl, pyridazinyl, pirazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, tetrazolyl, thiadiazolyl, oxadiazolyl, triazinyl, triazolyl, thienyl, pyrrolyl, pyrrolinyl, furyl, azepinyl, benzopyranyl, benzothienyl, benzotriazolyl, indolyl, isoindolyl, quinolyl, isoquinolyl, cinnolyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridyl, 1,7-naphthyridyl, 1,6-naphthyridyl, 1,5-naphthyridyl, pyrido[2,3-d]pyrimidyl, thieno[2,3-b]pyridyl, pyrrolidinyl, imidazolidinyl, piperidyl, piperidino, piperazinyl, morpholino, hydroazepinyl, hydroindolyl, hydroisoindolyl, hydroquinolyl, hydroisoquinolyl and the like, with preference given to thienyl, imidazolyl and morpholino.

The heteroaryl at R' may be those exemplified above for heteroaryl and pyridyl, with preference given to pyridyl, thienyl, imidazolyl and morpholino.

The heteroaryl formed by R^8 and R^9 together with the adjacent nitrogen atom, the heteroaryl formed by R^{13} and R^{14} together with the adjacent nitrogen atom, and the heteroaryl formed by R and R^{10} (R^{10a} , R^{10b} , R^{10d}) together with the adjacent nitrogen atom may be, of the above-mentioned heteroaryl, that having one or more nitrogen atoms. Specific examples include pyrrolidinyl, imidazolidinyl, piperidino, piperadiny, morpholino, pyrazolyl, imidazolyl, tetrazolyl, triazolyl, pyrrolyl, pyrrolinyl, indolyl, hydroazepinyl, hydroindolyl, hydroisoindolyl, hydroquinolyl, hydroisoquinolyl and the like, with preference given to morpholino, piperidino, pyrrolidinyl and imidazolyl.

With regard to the heteroarylalkyl at R^1 , $R^{1'}$, R^8 , R^9 and R^{15} , the heteroaryl moiety is that exemplified above and the alkyl moiety is that exemplified above which has 1 to 4 carbon atoms. Specific examples include 2-thienylmethyl, 3-furylmethyl, 4-pyridylmethyl, 2-quinolylmethyl, 3-isoquinolylmethyl and the like, with preference given to 4-pyridylmethyl.

The benzene-condensed cycloalkyl at R is specifically tetrahydronaphthalene,

indane and the like, with preference given to tetrahydronaphthalene.

The halogen atom at R^8 and R^9 may be fluorine, chlorine, bromine or iodine.

The amino-protecting group at R^{10} , R^{10a} , R^{10b} , R^{10d} and R^{11} may be an optionally substituted aralkylidene such as benzylidene, 4-chlorobenzylidene, 4-nitrobenzylidene, salicylidene, α -naphthylidene, β -naphthylidene and the like; an optionally substituted aralkyl such as benzyl, 4-methoxybenzyl, 3,4-dimethoxybenzyl, 2-nitrobenzyl, 4-nitrobenzyl, benzhydryl, bis(4-methoxyphenyl)methyl, trityl and the like; an optionally substituted acyl such as formyl, acetyl, propionyl, butyryl, pivaloyl, 2-chloroacetyl, 2-bromoacetyl, 2-iodoacetyl, 2,2-dichloroacetyl, 2,2,2-trichloroacetyl, 2,2,2-trifluoroacetyl, phenylacetyl, phenoxyacetyl, benzoyl, 4-chlorobenzoyl, 4-methoxybenzoyl, 4-nitrobenzoyl, naphthylcarbonyl, adamantylcarbonyl and the like; an optionally substituted alkoxy carbonyl such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, t-butoxycarbonyl, pentyloxycarbonyl, isopentyloxycarbonyl, cyclohexyloxycarbonyl, 2-chloroethoxycarbonyl, 2-iodoethoxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2,2,2-trichloro-t-butoxycarbonyl, benzhydryloxycarbonyl, bis-(4-methoxyphenyl)methoxycarbonyl, phenacyloxycarbonyl, 2-trimethylsilylethoxycarbonyl, 2-triphenylsilylethoxycarbonyl, fluorenyl-9-methoxycarbonyl and the like; an optionally substituted alkenyloxycarbonyl such as vinyloxycarbonyl, 2-propenyloxycarbonyl, 2-chloro-2-propenyloxycarbonyl, 3-methoxycarbonyl-2-propenyloxycarbonyl, 2-methyl-2-propenyloxycarbonyl, 2-butenyloxycarbonyl, cinnamyloxycarbonyl and the like; phenoxy carbonyl; an optionally substituted aralkyloxycarbonyl such as benzyloxycarbonyl, 4-bromobenzyloxycarbonyl, 2-chlorobenzyloxycarbonyl, 3-chlorobenzyloxycarbonyl, 3,5-dimethoxybenzyloxycarbonyl, 4-methoxybenzyloxycarbonyl, 2-nitrobenzyloxycarbonyl, 4-nitrobenzyloxycarbonyl, 2-nitro-4,5-dimethoxybenzyloxycarbonyl, 3,4,5-trimethoxybenzyloxycarbonyl, phenethyloxycarbonyl and the like;

an optionally substituted lower alkylsilyl such as trimethylsilyl, t-butyltrimethylsilyl and the like;
 an optionally substituted alkylthiocarbonyl such as methylthiocarbonyl, ethylthiocarbonyl, butylthiocarbonyl, t-butylthiocarbonyl and the like;
 an optionally substituted aralkylthiocarbonyl such as benzylthiocarbonyl;
 an optionally substituted phosphoryl such as dicyclohexylphosphoryl, diphenylphosphoryl, dibenzylphosphoryl, di-(4-nitrobenzyl)phosphoryl, phenoxyphenylphosphoryl and the like; and
 an optionally substituted phosphinyl such as diethylphosphinyl, diphenylphosphinyl and the like. It may be phthaloyl where appropriate. Preferred is aralkyloxycarbonyl and more preferred is benzyloxycarbonyl.

Each of the optionally substituted groups may be substituted by one or more substituents. The groups to be used as the substituents are explained in the following.

The alkyl may be that exemplified above which has 1 to 4 carbon atoms.

The alkoxy may be that exemplified above which has 1 to 4 carbon atoms.

The alkoxycarbonyl and halogen atom may be those exemplified above.

The heteroaryl may be those exemplified above for R'.

The alkylamino is that wherein the alkyl moiety is the above-mentioned alkyl having 1 to 4 carbon atoms. Specific examples of the alkylamino include methylamino, ethylamino, propylamino, butylamino, dimethylamino, diethylamino and the like.

The alkylthio is that wherein the alkyl moiety is the above-mentioned alkyl having 1 to 4 carbon atoms. Specific examples of the alkylthio include methylthio, ethylthio, propylthio, butylthio and the like.

The alkylsulfinyl is that wherein the alkyl moiety is the above-mentioned alkyl having 1 to 4 carbon atoms. Specific examples of the alkylsulfinyl include methylsulfinyl, ethylsulfinyl, propylsulfinyl, butylsulfinyl and the like.

The alkylsulfonyl is that wherein the alkyl moiety is the above-mentioned alkyl having 1 to 4 carbon atoms. Specific examples of the alkylsulfonyl include methylsulfonyl, ethylsulfonyl, propylsulfonyl, butylsulfonyl and the like.

The alkenyloxy is that wherein the alkenyl moiety is the above-mentioned

alkenyl having 2 to 4 carbon atoms. Specific examples of the alkenyloxy include ethenyloxy, propenyloxy, butenyloxy and the like.

The acyl may be those exemplified above which has 1 to 4 carbon atoms.

The acyloxy is that wherein the acyl moiety is the above-mentioned acyl having 1 to 4 carbon atoms. Specific examples of the acyloxy include formyloxy, acetyloxy, propionyloxy, butyryloxy, isobutyryloxy and the like, with preference given to acetyloxy.

The acylthio is that wherein the acyl moiety is the above-mentioned acyl having 1 to 4 carbon atoms. Specific examples of the acylthio include formylthio, acetylthio, propionylthio, butyrylthio, isobutyrylthio and the like, with preference given to acetylthio.

The acylamino is that wherein the acyl moiety is the above-mentioned acyl having 1 to 4 carbon atoms. Specific examples of the acylamino include formylamino, acetylamino, propionylamino, butyrylamino and the like, with preference given to acetylamino.

The alkoxycarbonyl is that wherein the alkoxy moiety is the above-mentioned alkoxy having 1 to 4 carbon atoms. Specific examples of the alkoxycarbonyl include methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl and the like, with preference given to ethoxycarbonyl.

The arylsulfinyl is that wherein the aryl moiety is the above-mentioned aryl. Specific examples of the arylsulfinyl include phenylsulfinyl, naphthylsulfinyl, biphenylsulfinyl and the like.

The aralkyloxy is that wherein the arylalkyl moiety is the above-mentioned arylalkyl. Specific examples of the aralkyloxy include benzyloxy, phenethyloxy, phenylpropyloxy, phenylbutyloxy, naphthylmethyloxy, biphenylmethyloxy and the like.

The pharmaceutically acceptable salts include, but not limited to, alkali metal salts such as sodium salt, potassium salt, secium salt and the like; alkaline earth metals such as calcium salt, magnesium salt and the like; organic amine salts such as triethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt and the like; inorganic acid salts such as hydrochloride, hydrobromide, sulfate,

phosphate and the like; organic acid salts such as formate, acetate, trifluoroacetate, malate, tartrate and the like; sulfonates such as methanesulfonate, benzenesulfonate, p-toluenesulfonate, and the like; amino acid salts such as arginate, asparagine, glutamate and the like.

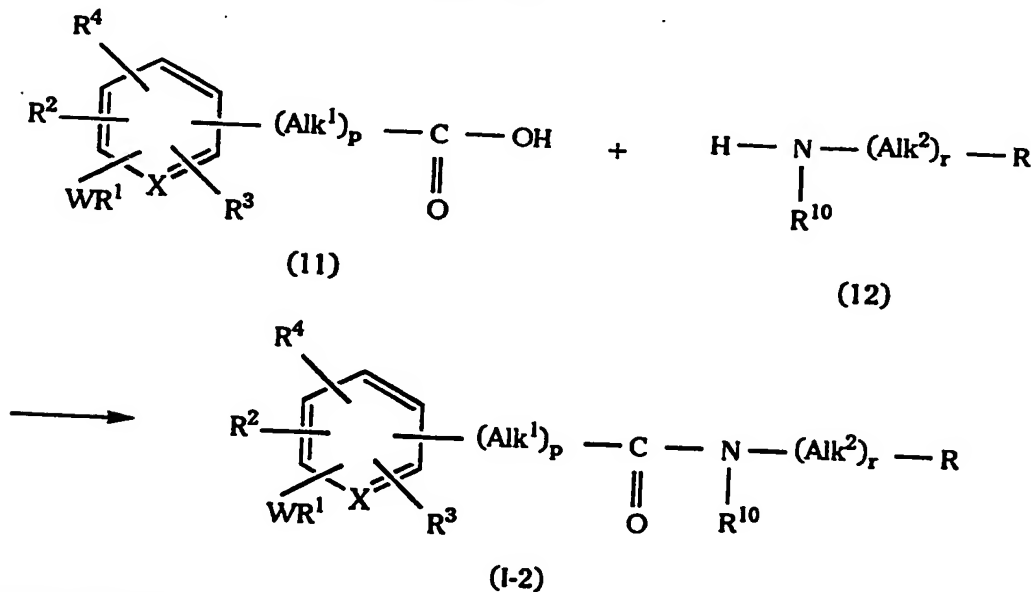
The present invention encompasses various isomers of respective compounds, prodrugs and the like.

In the present invention, Compounds (Ia), (Ib), (Ic), (Id) and (Ie) are encompassed in Compound (I). These compounds are explained together as Compound (I) in the following.

While the Compound (I) can be produced as in the following, the production method is not limited to those exemplified below.

Production Method 1: Compound of the formula (I) wherein q is 1 and Y is $-\text{CONR}^{10}-$

The present method comprises conversion of Compound (11) to an activated carboxylic acid derivative and reaction of the thus-obtained derivative with Compound (12) to give Compound (I-2).



wherein each symbol is as defined above.

Examples of the activated carboxylic acid derivative include acid halides obtained by the treatment of the carboxylic acids with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride and the like;

activated esters obtained by condensation of the carboxylic acids with N-hydroxybenzotriazole, N-hydroxysuccinimide and the like using a condensation agent such as dicyclohexylcarbodiimide (DCC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) hydrochloride and the like; and mixed acid anhydrides obtained by reaction of the carboxylic acid with ethyl chlorocarbonate, pivaloyl chloride, isobutyl chlorocarbonate and the like. Active esters derived from acids by the treatment with N-hydroxybenzotriazole using a condensing agent such as WSC hydrochloride are preferably used.

In the above reactions, a base may be used if necessary.

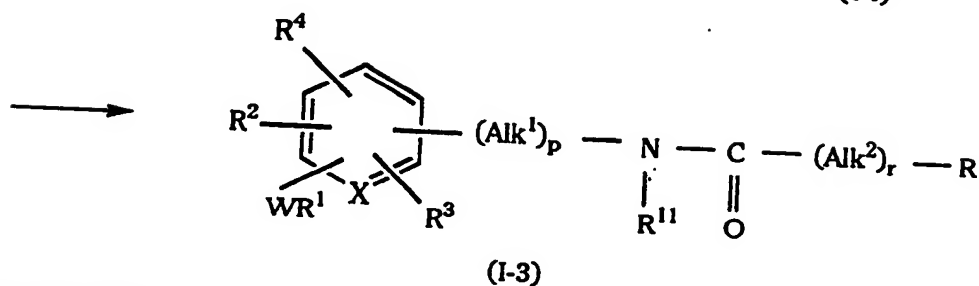
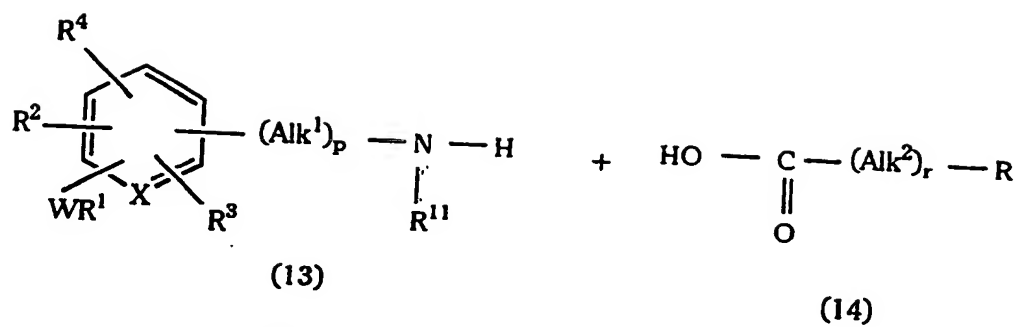
As the base, usable are, for example, organic amines such as triethylamine, pyridine, N-methylmorpholine and the like, with preference given to triethylamine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to dimethylformamide.

The reaction temperature is generally 0°C - 100°C, preferably 0°C - 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-12 hr.

Production Method 2: Compound of the formula (I) wherein q is 1 and Y is -NR¹¹CO-

The present method comprises conversion of Compound (14) to an activated carboxylic acid derivative and reaction of the thus-obtained derivative with Compound (13) in a suitable solvent in the presence of a suitable base to give Compound (I-3).

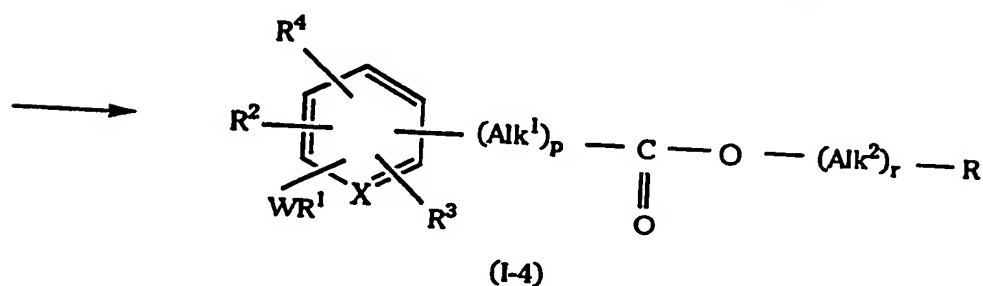
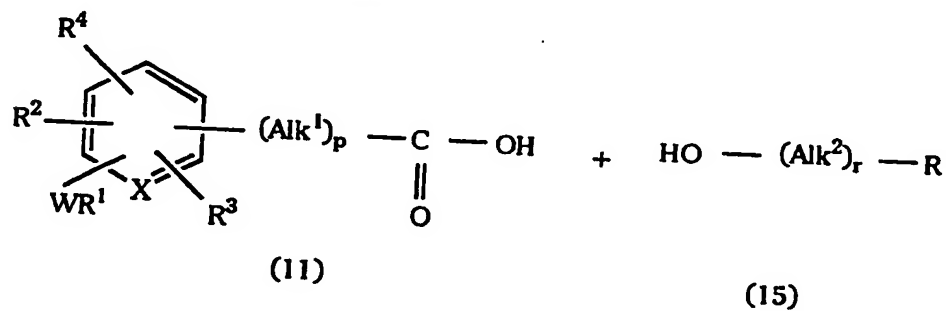


wherein each symbol is as defined above.

The activated carboxylic acid derivative, base, solvent and respective reaction temperature and time in the instant method are the same as those in Production Method 1.

Production Method 3: Compound of the formula (I) wherein q is 1 and Y is -COO-

The present method comprises conversion of Compound (11) to activated carboxylic acid derivatives and reaction of the thus-obtained derivatives with Compound (15) to give Compound (I-4).



wherein each symbol is as defined above.

Examples of the activated carboxylic acid derivative include acid halides obtained by the treatment of the carboxylic acid with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride and the like; active esters obtained by the treatment of the carboxylic acid with N-hydroxybenzotriazole, N-hydroxysuccinimide and the like, in the presence of a condensation agent such as DCC, WSC hydrochloride and the like; and mixed acid anhydrides obtained by the treatment of the carboxylic acid with ethyl chlorocarbonate, pivaloyl chloride, isobutyl chlorocarbonate and the like. An active ester obtained by using a condensing agent such as WSC hydrochloride is preferably used.

In the above reaction, a base may be used if necessary.

The representative bases are, for example, organic amines such as triethylamine, pyridine, N-methylmorpholine and the like, with preference given to pyridine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to the use of the above-mentioned base as a solvent.

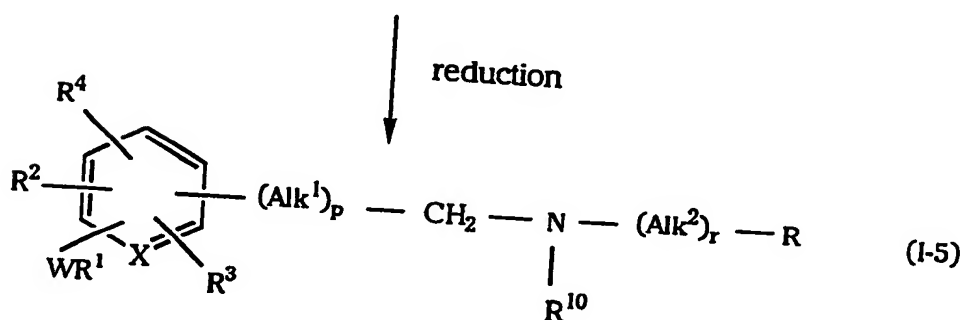
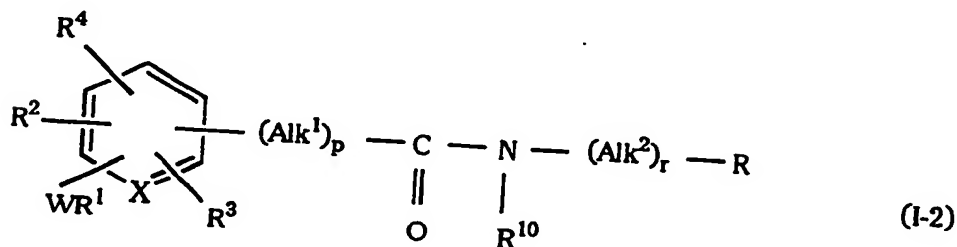
The reaction temperature is generally 0°C - 100°C, preferably 0°C - 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-12 hr.

Alternatively, Compound (I-4) is produced by the condensation of Compound (11) with Compound (15) by the action of acid catalysts.

The representative acid catalysts are, for example, a mineral acid such as hydrochloric acid, sulfuric acid, nitric acid and the like, or an organic acid such as acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like.

Production Method 4: Compound of the formula (I) wherein q is 1 and Y is $-\text{CH}_2\text{NR}^{10}-$.

The present method comprises reduction of Compound (I-2) obtained in Production Method 1, using a suitable reducing agent in a suitable solvent to give Compound (I-5).



wherein each symbol is as defined above.

Examples of the reducing agents include, for example, LiAlH_4 , LiBH_4 , NaBH_4 , diisobutylaluminum hydride (DIBAL), reduced aluminum (Red-Al) and the like, with preference given to LiAlH_4 .

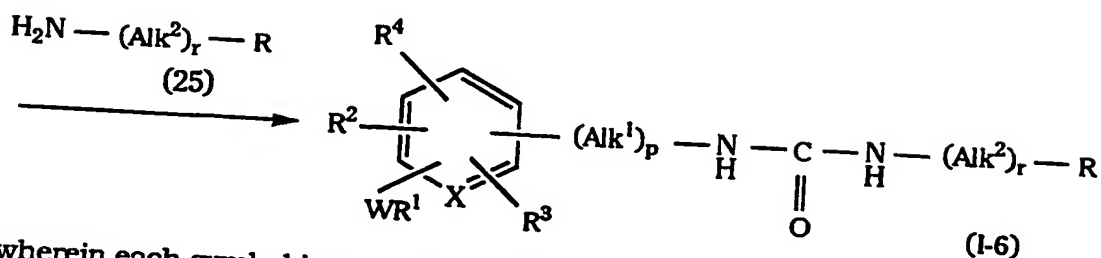
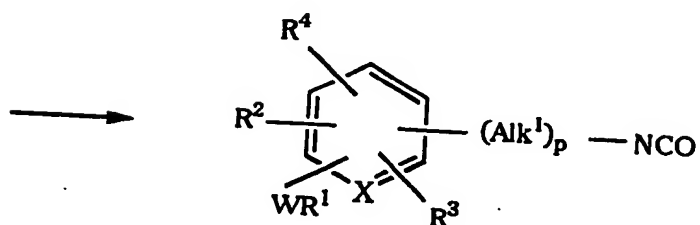
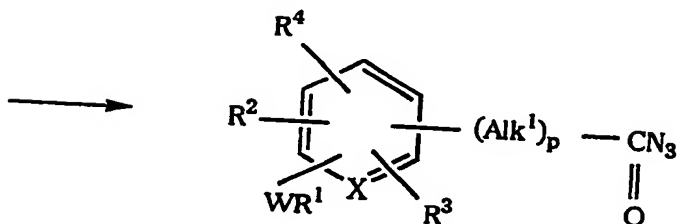
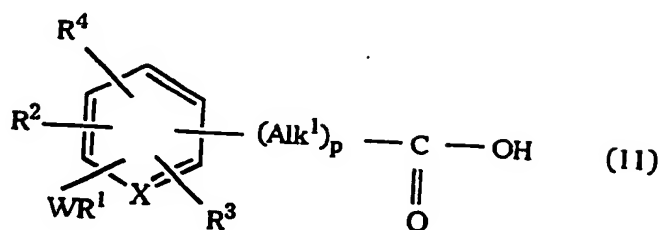
Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to ether solvents which is more preferably tetrahydrofuran.

The reaction temperature is generally from -30°C to 100°C , preferably 0°C - 50°C , and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

Production Method 5: Compound of the formula (I) wherein q is 1 and Y is -NHCONH-

The present method comprises Curtius rearrangement of acid azide derived from Compound (11) and reaction of the thus-obtained isocyanate with

Compound (25) to give Compound (I-6).



wherein each symbol is as defined above.

The Curtius rearrangement converts acyl azide to isocyanate by thermal rearrangement.

The acyl azide may be synthesized by ① a method wherein carboxylic acid is reacted with diphenylphosphoric azide in the presence of a base, ② a method wherein carboxylic acid is converted to hydrazide via ester and the thus-obtained hydrazide is reacted with nitrous acid or alkyl ester thereof, ③ a method wherein carboxylic acid is converted to acid chloride and the thus-obtained acid chloride is reacted with sodium azide, ④ a method wherein mixed acid anhydride is reacted with sodium azide, or other method.

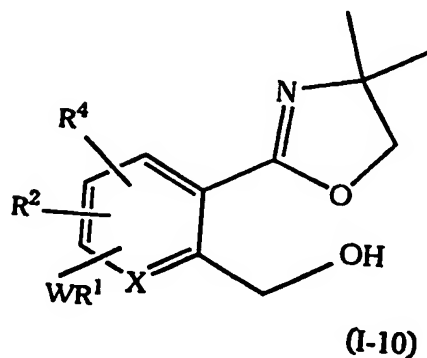
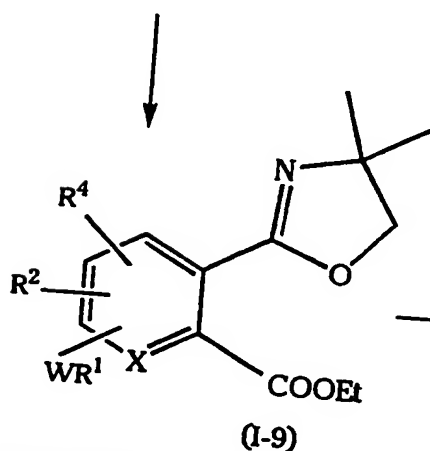
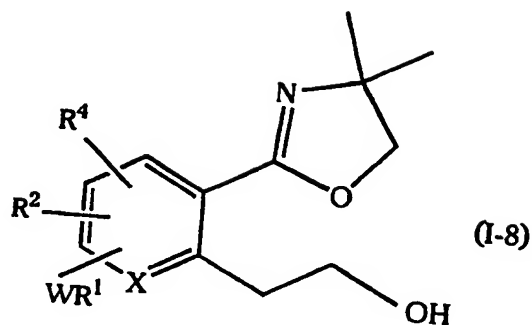
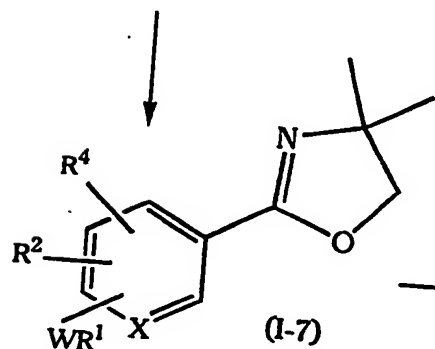
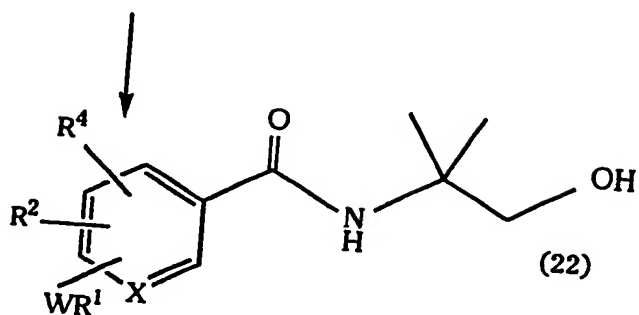
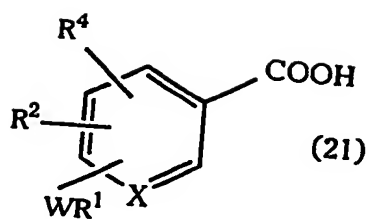
As the base, exemplified are triethylamine, pyridine, potassium hydride, sodium hydride, N-methylmorpholine and the like, with preference given to triethylamine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme, dioxane and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably dioxane.

The reaction temperature is generally 0°C - 150°C, preferably 0°C - 80°C, and the reaction time is generally 15 min-6 hr, preferably 1-3 hr.

Production Method 6: Compound of the formula (I) wherein $p=q=r=0$ and R is a group of the formula (i) which may be substituted by one or more substituent(s)

The compound wherein R is 4,4-dimethyl-4,5-dihydrooxazoliny is exemplified here.



wherein each symbol is as defined above.

(1) According to the present method, Compound (21) is converted to the acid halide by thionyl halide, and the thus-obtained acid halide is then reacted with 2-amino-2-methylpropanol to give Compound (22).

Examples of thionyl halide include thionyl chloride, thionyl bromide and the like.

The instant step can be performed, besides conversion to acid halide, by using a suitable condensing agent.

Examples of the condensing agent include DCC, WSC hydrochloride, pivaloyl chloride, ethoxycarbonyl chloride and the like. As an additive, hydroxybenzotriazole (HOBT), N-hydroxysuccinimide (NBS), pyridine, triethylamine and the like may be used as appropriate upon selection.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to a halogen solvent which is more preferably dichloromethane.

The reaction temperature is generally 0°C - 100°C, preferably 0°C - 40°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(2) The Compound (22) obtained in (1) is reacted with a suitable dehydrating agent to give Compound (I-7).

Examples of the dehydrating agent include thionyl chloride, POCl₃, phosphorus pentachloride, diphosphorus pentoxide, acetic anhydride, zinc chloride, titanium tetrachloride and the like, with preference given to thionyl chloride.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to the reaction without solvent.

The reaction temperature is generally 0°C - 100°C, preferably 10°C - 50°C,

and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(3) The Compound (I-7) obtained in (2) is treated with a suitable base and reacted with ethylene oxide to give Compound (I-8).

The base may be, for example, lithium diisopropylamide (LDA), n-butyllithium, s-butyllithium, t-butyllithium, lithium hexamethyldisilazane (LiHMDS), sodium hexamethyldisilazane (NaHMDS), potassium hexamethyldisilazane (KHMDS), sodium hydride, potassium hydride, EtMgBr, (i-Pr)₂NMgBr and the like, with preference given to n-butyllithium.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably 1,2-dimethoxyethane.

The reaction temperature is generally from -100°C to 100°C, preferably from -100°C to 0°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(4) The Compound (I-7) obtained in (2) is treated with a suitable base and reacted with a suitable carbonic acid ester to give Compound (I-9).

The base may be, for example, LDA, n-butyllithium, s-butyllithium, t-butyllithium, LiHMDS, NaHMDS, KHMDS, sodium hydride, potassium hydride, EtMgBr, (i-Pr)₂NMgBr and the like, with preference given to n-butyllithium.

The carbonic acid ester may be, for example, ethyl chlorocarbonate, diethyl carbonate and the like, with preference given to ethyl chlorocarbonate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably 1,2-dimethoxyethane.

The reaction temperature is generally from -100°C to 100°C, preferably from -78°C to 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(5) The Compound (I-9) obtained in (4) is reacted with a suitable reducing agent to

give Compound (I-10).

Examples of the reducing agent include LiAlH_4 , LiBH_4 , NaBH_4 , DIBAL, Red-Al and the like, with preference given to LiAlH_4 .

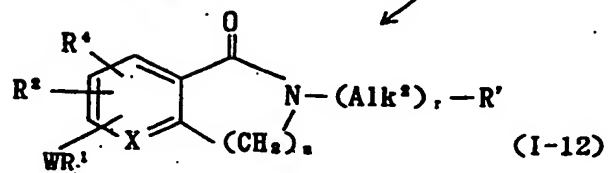
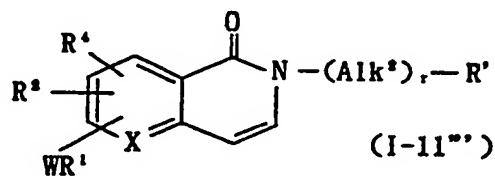
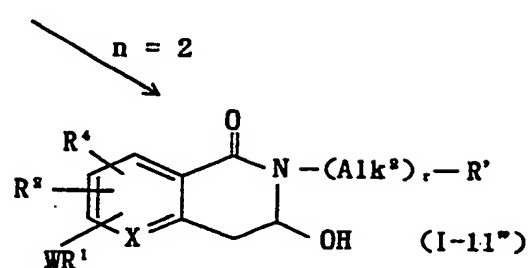
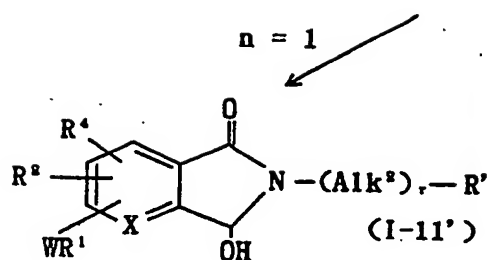
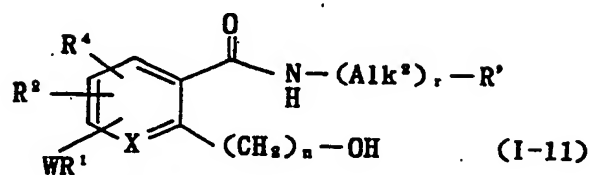
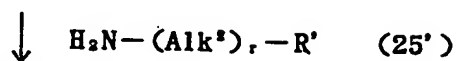
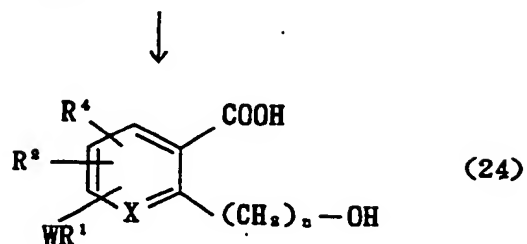
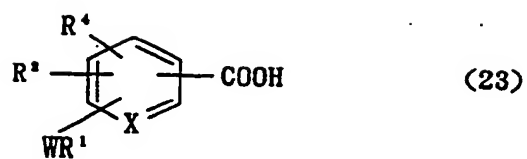
Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably tetrahydrofuran.

The reaction temperature is generally -30°C - 100°C , preferably 0°C - 50°C , and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

Production Method 7: Compound of the formula (I) wherein $p=0$, $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$ and R^3 and R^{10} in combination form a condensed ring together with A ring

This production method is explained in the following Production Methods 7-1 - 7-6.

Production Method 7-1: Compound of the formula (I) wherein $p=0$, $q=1$, Y is $-\text{CONR}^{10}-$ and R^3 and R^{10} in combination form $-\text{CH}_2\text{CH}_2-$, $-\text{CH}_2-$, $-\text{CH}=\text{CH}-$, $-\text{CHOH}-$ or $-\text{CH}_2\text{CHOH}-$



wherein n is 1 or 2 and other symbols are as defined above.

(1) According to this method, the carbon adjacent to the carbon bonded to the carboxyl group of Compound (23) is alkylated to give Compound (24).

The carboxylic acid is converted to oxazoline (I-7), treated with a suitable base and alkylated with ethylene oxide to give Compound (I-8). The hydrolysis of the thus-obtained compound by a conventional method gives Compound (24) wherein n is 2.

When the Compound (I-7) is alkylated with a base and ethyl chlorocarbonate to give Compound (I-9), and this compound is treated with a suitable reducing reagent, Compound (I-10) is obtained. By hydrolysis of Compound (I-10) by a conventional method, Compound (24) wherein n is 1 is derived.

The reaction conditions are the same as those in Production Method 6, (3), (4) and (5).

(2) Then, Compound (24) is converted to an activated carboxylic acid derivative and condensed with Compound (25) to give Compound (I-11).

Examples of the activated carboxylic acid derivative include acid halides obtained by treatment of the carboxylic acid with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride and the like; active esters obtained by the treatment of the carboxylic acid with N-hydroxybenzotriazole, N-hydroxysuccinimide and the like, in the presence of a condensing agent such as DCC, WSC hydrochloride and the like; and mixed acid anhydrides obtained by the treatment of the carboxylic acid with ethyl chlorocarbonate, pivaloyl chloride, isobutyl chlorocarbonate and the like. An active ester derived from the carboxylic acid by the treatment with N-hydroxybenzotriazole and WSC hydrochloride as the condensing agent is preferably used.

In the above reaction, a base may be present as necessary.

As the base, usable are, for example, organic amine such as triethylamine, pyridine, N-methylmorpholine and the like, with preference given to triethylamine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the

like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to dimethylformamide.

The reaction temperature is generally 0°C - 100°C, preferably 0°C - 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-12 hr.

(3) The Compound (I-11) can be dehydrated to give Compound (I-12).

The dehydration is performed in the presence of an acid which is exemplified by Lewis acid such as aluminum chloride, tin chloride, zinc chloride, copper chloride, copper bromide, iron chloride, boron trifluoride-diethyl ether, titanium tetrachloride and the like; mineral acid such as hydrochloric acid, sulfuric acid, nitric acid and the like; and organic acid such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like, with preference given to p-toluenesulfonic acid.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to toluene.

The reaction temperature is generally 0°C - 200°C, preferably 60°C - 120°C, and the reaction time is generally 3-48 hr, preferably 6-12 hr.

(3') When the aforementioned dehydration using an acid catalyst does not proceed smoothly, the hydroxyl group of the 2-position alkyl of Compound (I-11) may be oxidized to give an aminor (I-11' when n is 1) or an aminor (I-11" when n is 2). A following reduction of the thus-obtained aminor with a suitable reducing agent gives Compound (I-12).

An electrophile for oxidation may be, for example, acetic anhydride, trifluoroacetic anhydride, sulfur trioxide-pyridine complex (SO₃-Py), diphosphorus pentoxide, (COCl)₂ and the like, with preference given to SO₃-Py.

In addition, an additive such as dimethyl sulfoxide, triethylamine and the like may be used. Moreover, a chromic oxidizing agent such as pyridinium chloro-

chromate (PCC), pyridinium dichromate (PDC) and the like may be used.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to dimethyl sulfoxide.

The reaction temperature is generally -78°C - 30°C , preferably 10°C - 20°C , and the reaction time is generally 15 min-24 hr, preferably 1-3 hr.

Examples of the reducing reagent include sodium borohydride, sodium cyanoborohydride, lithium borohydride, triethylsilane, trimethylsilane, diphenylsilane, phenylsilane, trichlorosilane, trimethylsilane and the like, with preference given to triethylsilane.

The reduction may be carried out in the presence of a suitable acid.

Examples of the acid include trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like, with preference given to trifluoroacetic acid.

The reaction temperature is generally from -10°C to 100°C , preferably 0°C - 30°C , and the reaction time is generally 15 min-48 hr, preferably 30 min-3 hr.

This reduction may be also performed by catalytic hydrogenation.

(3rd) In the above-mentioned case wherein n is 2, amination (I-11st) is treated with an acid in a solvent and dehydrated to give Compound (I-11st) which is one of the objective compounds. The Compound (I-11st) is successively reduced in a suitable solvent to give Compound (I-12) wherein n is 2.

The acid to be used in the above-mentioned dehydration is exemplified by Lewis acid such as aluminum chloride, tin chloride, zinc chloride, copper chloride, copper bromide, iron chloride, boron trifluoride-diethyl ether, titanium tetrachloride and the like; mineral acid such as hydrochloric acid, sulfuric acid, nitric acid and the like; and organic acid such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like, with preference given to

hydrochloric acid.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to chloroform.

The reaction temperature is generally 0°C - 200°C, preferably 60°C - 120°C, and the reaction time is generally 3-48 hr, preferably 6-12 hr.

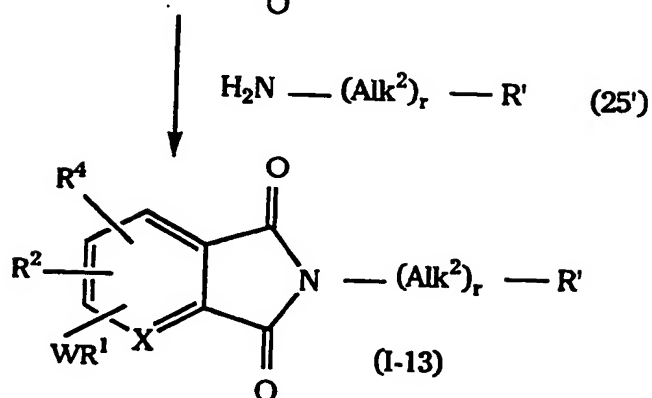
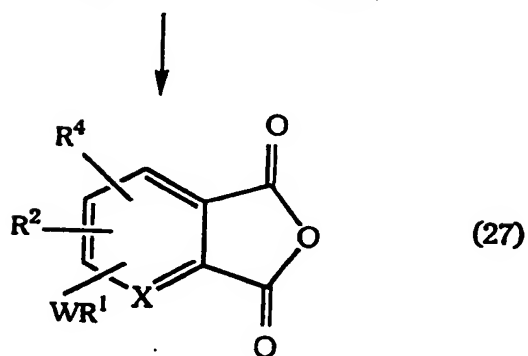
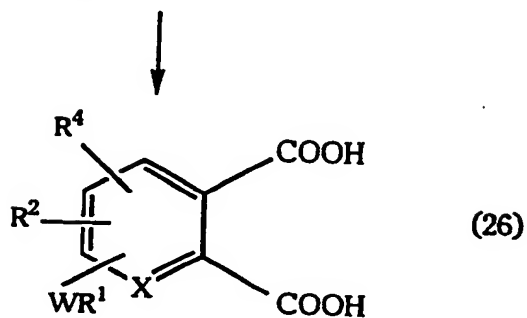
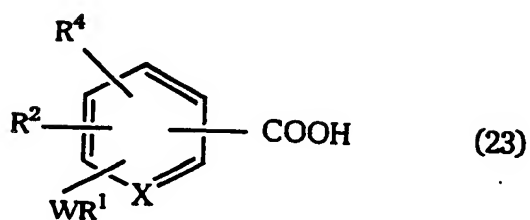
The reduction catalyst to be used in the above-mentioned reduction may be, for example, palladium-carbon, palladium hydroxide-carbon, Raney nickel and the like, which is preferably palladium-carbon.

Examples of the suitable solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, acetonitrile, acetone and the like; alcohol solvents such as methanol, ethanol and the like; and acids such as hydrochloric acid, acetic acid and the like, with preference given to acetic acid.

The reaction is performed under high pressure conditions in a hydrogen atmosphere, which is generally 1-4 kgf/cm², preferably 3 kgf/cm².

The reaction temperature is generally 0°C - 100°C, preferably 50°C - 60°C, and the reaction time is generally 1-48 hr, preferably 1-20 hr.

Production Method 7-2: Compound of the formula (I) wherein p=0, q=1, Y is -CONR¹⁰- and R⁹ and R¹⁰ in combination show -CO- and form a condensed ring with A ring



wherein each symbol is as defined above.

(1) In the same manner as in Production Method 7-1, the carbon adjacent to the carbon bearing carboxyl group of Compound (23) is acylated to give Compound (26).

The acylating agent may be, for example, ethyl chlorocarbonate,

carbon dioxide and the like, with preference given to ethyl chloro-carbonate.

When oxazoline is used as a carboxylic acid equivalent, carboxylic acid can be regenerated by a conventional method after acylation.

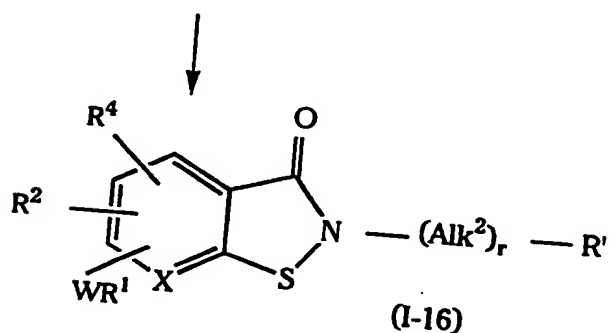
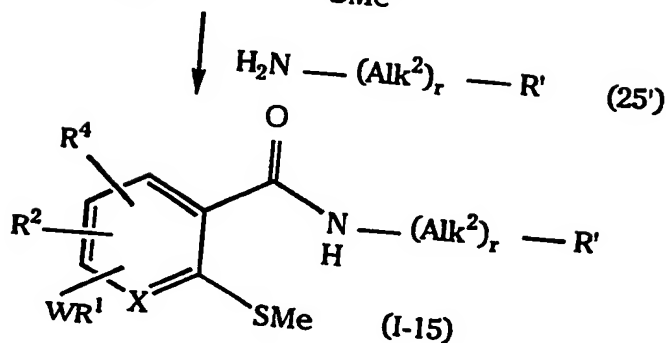
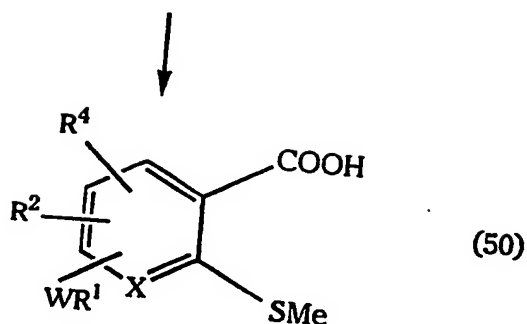
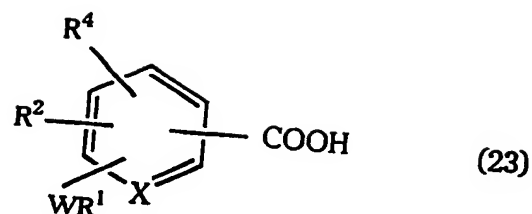
(2) The Compound (26) obtained in (1) can be converted to Compound (27) by a conventional method.

(3) The Compound (27) obtained in (2) is subjected to thermal dehydration condensation with Compound (25') to give Compound (I-13).

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to toluene.

The reaction temperature is generally 0°C - 200°C, preferably 100°C - 130°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

Production Method 7-3: Compound of the formula (I) wherein $p=0$, $q=1$, Y is - CONR¹⁰- and R³ and R¹⁰ in combination show -S- and form a condensed ring with A ring



wherein each symbol is as defined above.

(1) With this procedure, in the ring, methylthio group is introduced into the carbon adjacent to the carbon bearing carboxyl group of Compound (23) to give Compound (50).

When, for example, carboxylic acid is converted to oxazoline (I-7) and oxazoline (I-7) is treated with a suitable base and reacted with dialkylsulfide,

Compound (50) is obtained. When oxazoline is used as a carboxylic acid equivalent, carboxylic acid can be regenerated by a conventional method after introduction of methylthio group.

The base to be used may be, for example, LDA, n-butyllithium, s-butyllithium, t-butyllithium, LiHMDS, NaHMDS, KHMDS, sodium hydride, potassium hydride, EtMgBr, (i-Pr)₂NMgBr and the like, with preference given to n-butyllithium.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably 1,2-dimethoxyethane.

(2) Then, Compound (50) is converted to an activated carboxylic acid derivative and condensed with Compound (25') to give Compound (I-15).

Examples of the activated carboxylic acid derivative include acid halides obtained by treatment of the carboxylic acid with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride and the like; active esters obtained by condensation of the carboxylic acid with N-hydroxybenzotriazole, N-hydroxysuccinimide and the like using a condensing agent such as DCC, WSC hydrochloride and the like; and mixed acid anhydrides obtained by reaction of the carboxylic acid with ethyl chlorocarbonate, pivaloyl chloride, isobutyl chlorocarbonate and the like. An active ester obtained by condensation of the carboxylic acid with N-hydroxybenzotriazole using WSC hydrochloride as a condensing agent is preferably used.

In the above reaction, a base may be present as necessary.

As the base, usable are, for example, organic amine such as triethylamine, pyridine, N-methylmorpholine and the like, with preference given to triethylamine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like;

and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to dimethylformamide.

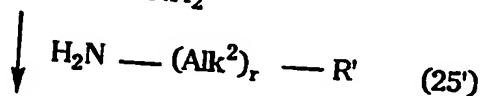
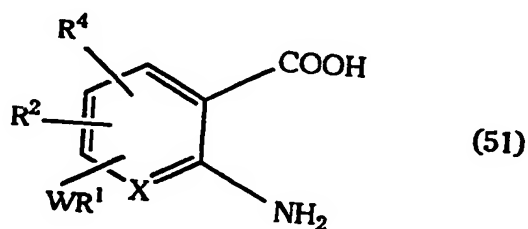
The reaction temperature is generally 0°C - 100°C, preferably 0°C - 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-12 hr.

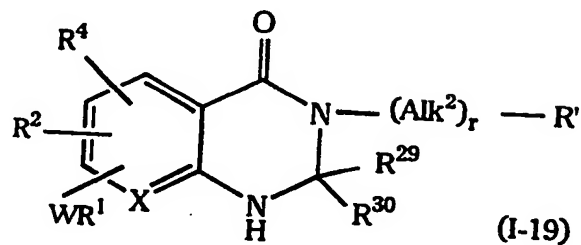
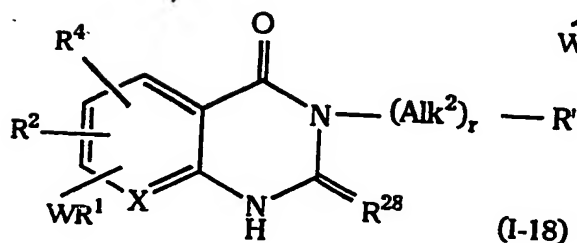
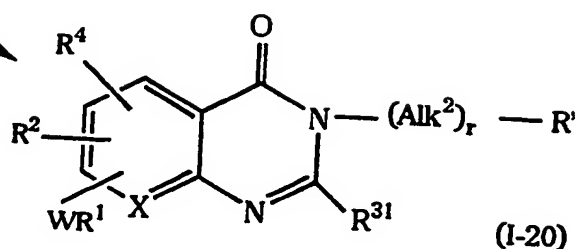
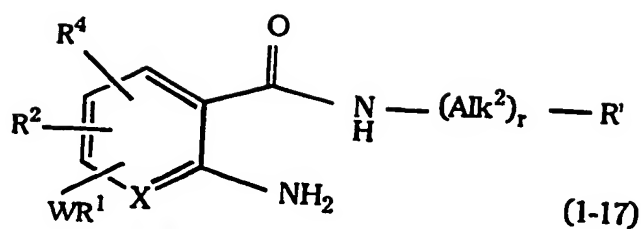
(3) The Compound (I-15) is cyclized in the presence of N-chlorosuccinimide to give Compound (I-16).

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to dichloromethane.

The reaction temperature is generally 0°C - 200°C, preferably 0°C - 30°C, and the reaction time is generally 3-48 hr, preferably 6-12 hr.

Production Method 7-4: Compound of the formula (I) wherein $p=0$, $q=1$, Y is -CONR¹⁰- and R³ and R¹⁰ in combination show -NHCR²⁸-, -NHCR²⁹R³⁰- or -N=CR³¹- and form a condensed ring with A ring





wherein each symbol is as defined above.

(1) The activated carboxylic acid derivative (51) is condensed with Compound (25') to give Compound (I-17).

Examples of the activated carboxylic acid derivative include acid halides obtained by treatment of the carboxylic acids with thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, oxalyl chloride and the like; activated esters obtained by condensation of the carboxylic acids with N-hydroxybenzotriazole, N-hydroxysuccinimide and the like using a condensation agent such as DCC, WSC hydrochloride and the like; and mixed acid anhydrides obtained by the reaction of the carboxylic acid with ethyl chlorocarbonate, pivaloyl chloride, isobutyl chlorocarbonate and the like. Active esters derived from the

carboxylic acid by treatment with N-hydroxybenzotriazole and WSC hydrochloride as a condensing agent is preferably used.

In the above reactions, a base may be used if necessary.

As the base, usable are, for example, organic amines such as triethylamine, pyridine, N-methylmorpholine and the like, with preference given to triethylamine.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to dimethylformamide.

The reaction temperature is generally 0°C - 100°C, preferably 0°C - 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-12 hr.

(2) Then Compound (I-17) can be converted to Compound (I-18), Compound (I-19) or Compound (I-20) by condensing with a carbon unit compound in the presence of an acid.

The carbon unit compound is, for example, triphosgene when R²⁸ in Compound (I-18) is oxygen atom, and carbon disulfide when R²⁸ is sulfur atom. It is acetone when R²⁹ and R³⁰ in Compound (I-19) are both methyl, dimethylformamide dimethylacetal when R³¹ in Compound (I-20) is hydrogen atom, and acetylacetone when R³¹ is methyl.

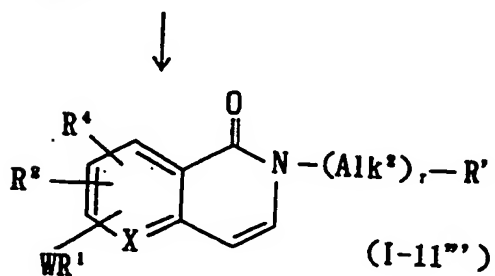
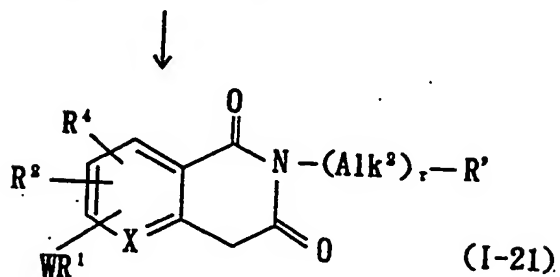
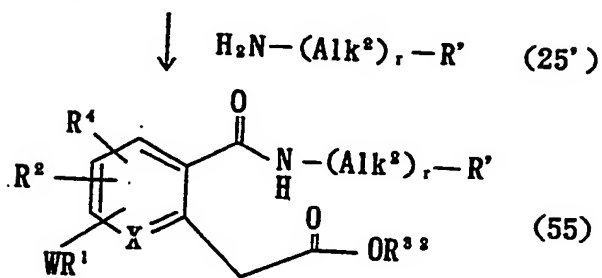
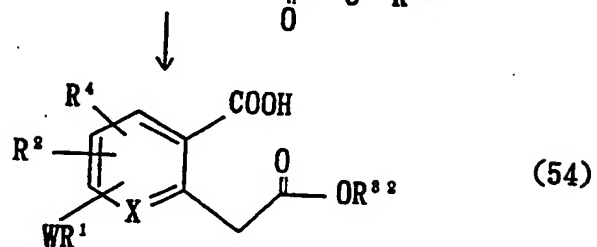
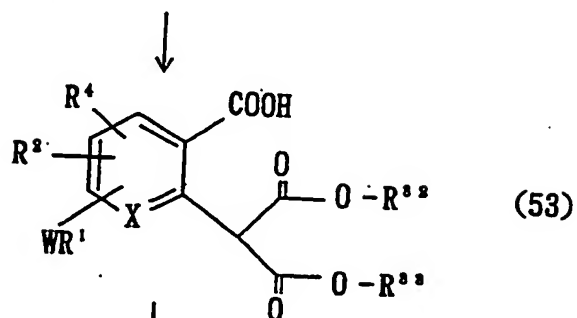
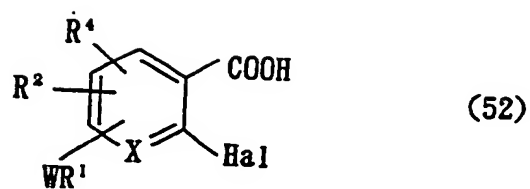
Examples of the acid include Lewis acid such as aluminum chloride, tin chloride, zinc chloride, copper chloride, copper bromide, iron chloride, boron trifluoride-diethyl ether, titanium tetrachloride and the like; mineral acid such as hydrochloric acid, sulfuric acid, nitric acid and the like; and organic acid such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like, with preference given to hydrochloric acid.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the

like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to chloroform.

The reaction temperature is generally 0°C - 200°C, preferably from room temperature to 100°C, and the reaction time is generally 3-48 hr, preferably 6-12 hr.

Production Method 7-5: Compound of the formula (I) wherein $p=0$, $q=1$, Y is -CONR¹⁰- and R³ and R¹⁰ in combination show -CH₂CO- or -CH=CH- and form a condensed ring with A ring



wherein Hal is halogen atom, R^{32} and R^{33} are the same or different and each is alkyl having 1 to 6 carbon atoms or benzyl and other symbols are as defined above.

(1) The Compound (52) is reacted with an activated ester compound in a suitable solvent in the presence of a metallic catalyst to give Compound (53).

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; and ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like, with preference given to toluene.

The metallic catalyst is exemplified by copper halide and the like, which is preferably copper bromide.

The activated ester can be formed by mixing alkyl malonate and the like with a suitable base.

A suitable base in this case is, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to sodium hydride.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 100°C , and the reaction time is generally 15 min-48 hr, preferably 30 min-3 hr.

(2) The Compound (53) is decarboxylated in a suitable solvent in the presence of a salt to give Compound (54).

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, water and the like, with preference given to a polar solvent which is more preferably a mixed solvent of water and dimethyl sulfoxide.

Examples of the salt include sodium chloride, sodium cyanide, lithium fluoride, lithium chloride, lithium iodide, lithium carbonate, potassium bromide, potassium chloride, potassium iodide, potassium cyanide, magnesium chloride and the like.

The reaction temperature is generally from 0°C to 300°C, preferably 100°C - 200°C, and the reaction time is generally 15 min-24 hr, preferably 30 min-3 hr.

(3) Using Compound (54) and Compound (25'), Compound (55) can be obtained in the same manner as in Production Method 7-1(2) by amide condensation.

(4) The Compound (55) is cyclized in a suitable solvent in the presence of a base to give Compound (I-21).

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to an alcohol solvent which is more preferably ethanol.

A suitable base is, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, potassium hydroxide, lithium hydroxide, sodium methoxide, sodium ethoxide, potassium t-butoxide and the like, with preference given to sodium ethoxide.

The reaction temperature is generally 0°C - 200°C, preferably 0°C - 150°C, and the reaction time is generally 15 min-24 hr, preferably 30 min-3 hr.

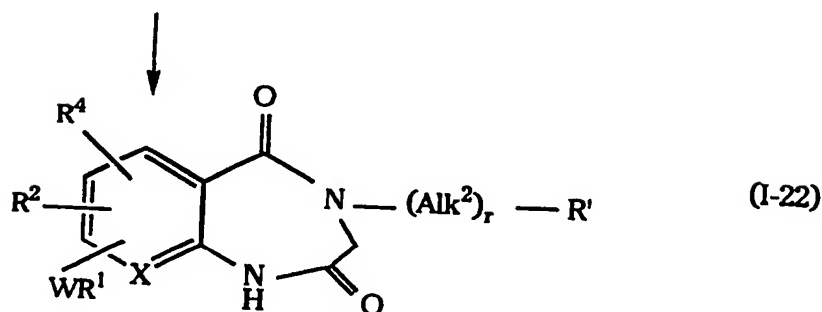
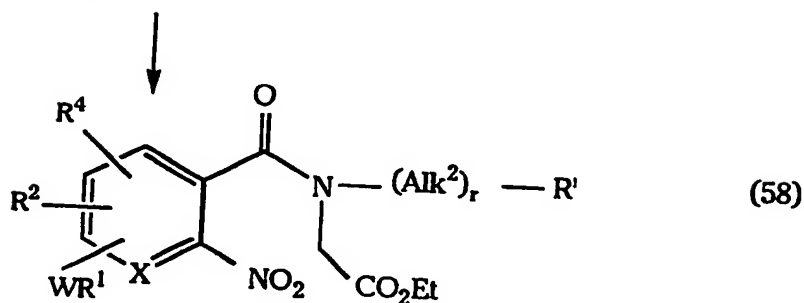
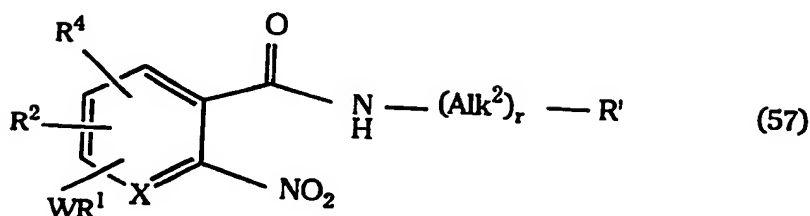
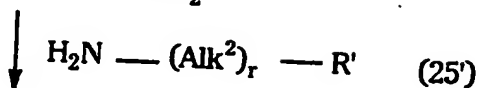
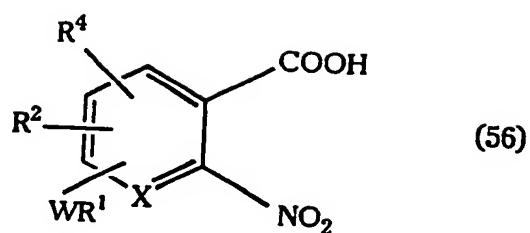
(5) The Compound (I-21) is reduced and dehydrated to give Compound (I-11').

Examples of the reducing agent include LiAlH_4 , LiBH_4 , NaBH_4 , DIBAL, Red-Al and the like, with preference given to LiAlH_4 .

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably tetrahydrofuran.

The reaction temperature is generally -30°C - 100°C, preferably 0°C - 50°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

Production Method 7-6: Compound of the formula (I) wherein $p=0$, $q=1$, Y is - CONR^{10} - and R^3 and R^{10} in combination form $-\text{NHCOCH}_2-$



wherein each symbol is as defined above.

(1) Using Compound (56) and Compound (25'), Compound (57) can be obtained in the same manner as in Production Method 7-1(2) by amide condensation.

(2) The Compound (57) is alkylated at the amide group with ethyl haloacetate such as ethyl bromoacetate in the presence of a base to give Compound (58).

A suitable base is, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate,

sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to sodium hydride.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to tetrahydrofuran.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 100°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(3) The Compound (58) is converted to Compound (I-22) by reduction of nitro group by a conventional method followed by cyclization.

The cyclization is performed in the presence of an acid which is exemplified by Lewis acid such as aluminum chloride, tin chloride, zinc chloride, copper chloride, copper bromide, iron chloride, boron trifluoride-diethyl ether, titanium tetrachloride and the like; mineral acid such as hydrochloric acid, sulfuric acid, nitric acid and the like; and organic acid such as trifluoroacetic acid, trichloroacetic acid, acetic acid, methanesulfonic acid, p-toluenesulfonic acid and the like, with preference given to p-toluenesulfonic acid.

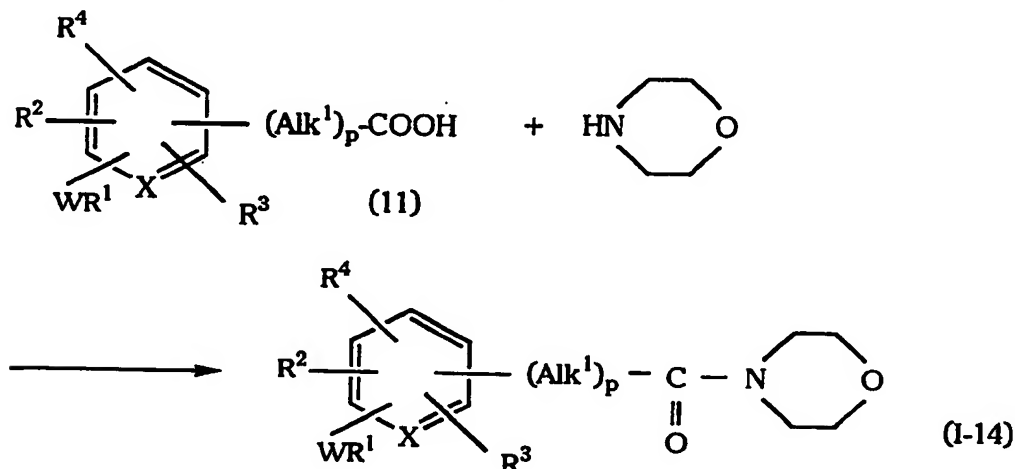
Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like, with preference given to toluene.

The reaction temperature is generally 0°C - 200°C , preferably 60°C - 120°C , and the reaction time is generally 3-48 hr, preferably 6-12 hr.

Production Method 8: Compound of the formula (I) wherein $r=0$, $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$ and R and R^{10} in combination form heteroaryl together with the adjacent nitrogen atom

The compound of the formula (I) wherein $r=0$, $q=1$, Y is $-\text{CONR}^{10}-$ and R and R^{10} in combination form morpholino together with the adjacent nitrogen atom is exemplified here.

The present method comprises converting Compound (11) to an activated carboxylic acid derivative and reacting the derivative with morpholine in a suitable solvent in the presence of a base to give Compound (I-14).



wherein each symbol is as defined above.

The activated carboxylic acid derivative, base, solvent and respective conditions of reaction temperature and reaction time in the instant method are the same as in Production Method 1.

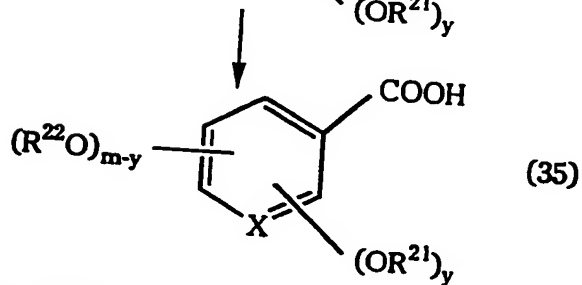
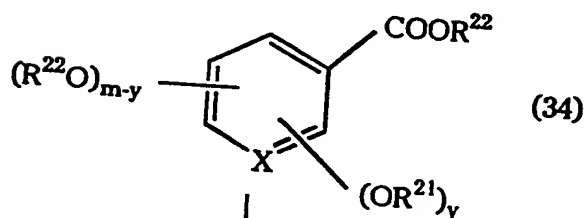
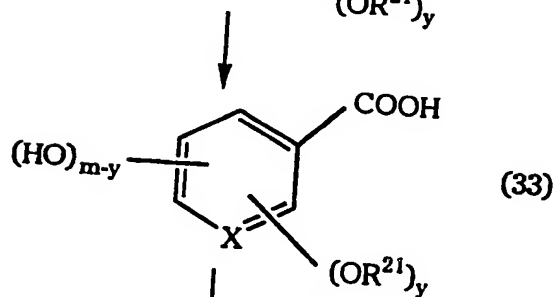
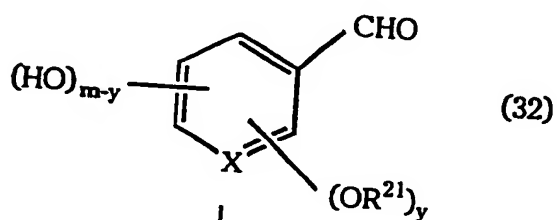
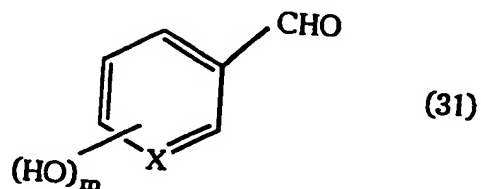
The compound wherein R and R^{10} in combination form other heteroaryl together with the adjacent nitrogen atom can be synthesized in the same manner as above except that the heteroaryl ring is used instead of morpholine as the starting compound.

The compound wherein Y is $-\text{CH}_2\text{NR}^{10}-$ can be synthesized by reducing the compound wherein Y is $-\text{CONR}^{10}-$ according to Production Method 4.

While Production Methods 1-8 have been explained in the above, a compound wherein R^2 and R^4 in combination form a condensed ring of the formula (II) with the A ring in the above Production Method can be synthesized in the same manner as in the above Production Method except that a compound having the condensed ring is used as a starting compound.

The Compound (11) to be used as the starting compound in Production Method 1 can be obtained, for example, as in the following Production Methods 1-A to 1-F.

Production Method 1-A



wherein R^{21} and R^{22} are each the same as those shown with regard to R^1 , T is

halogen atom, m and y are each 1, 2 or 3 and $m-y \geq 0$.

(1) Using Compound (31) as the starting material, the hydroxyl group is subjected to etherification with Compound (29) in the presence of a base to give Compound (32).

As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to lithium carbonate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to dimethylformamide.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 60°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(2) Then, the Compound (32) obtained in (1) is oxidized to give Compound (33).

The oxidizing agent to be used is exemplified by NaClO_2 , CrO_3 , $\text{K}_2\text{Cr}_2\text{O}_7$, KMnO_4 and the like.

As an additive, NaHPO_4 , KHPO_4 , amylene and the like may be used as appropriate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, acetic acid, water and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to t-

butanol.

(3) Then, the Compound (33) obtained in (2) is subjected to etherification with Compound (30) in the presence of a base to give Compound (34).

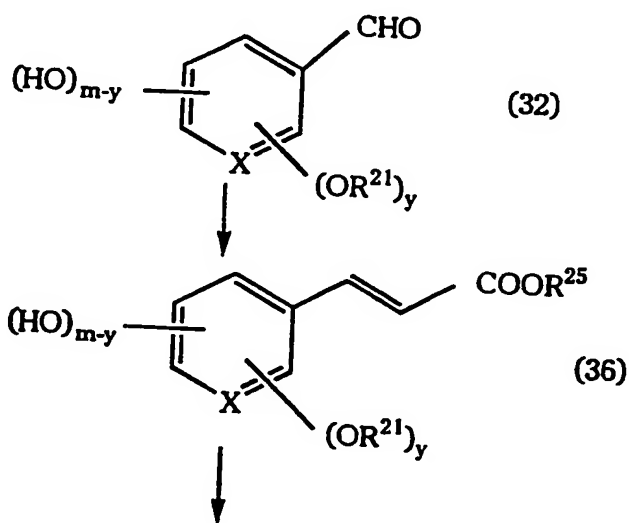
As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to potassium carbonate.

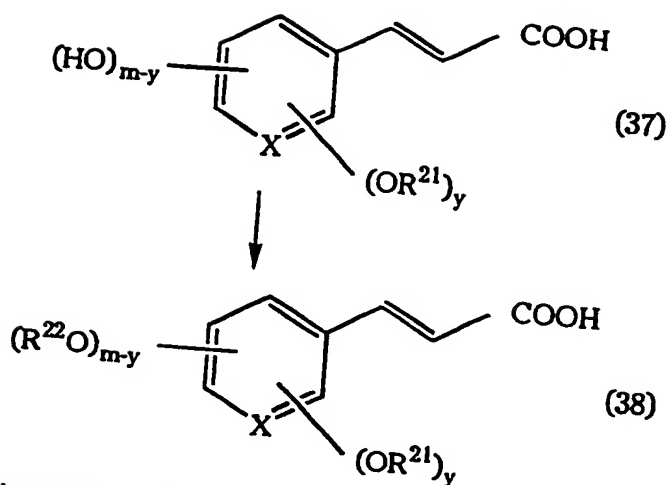
Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to dimethylformamide.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 60°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(4) The Compound (34) obtained in (3) is hydrolyzed in the presence of a base by a conventional method to give Compound (35).

Production Method 1-B





wherein R^{25} is alkyl having 1 to 6 carbon atoms and other symbols are as defined above.

(1) The Compound (32) obtained in Production Method 1-A(1) is subjected to Wittig reaction to give Compound (36).

Examples of Wittig reagent include methyl (triphenylphosphoranyliden)acetate, ethyl (triphenylphosphoranyliden)acetate, and the like, preferably methyl (triphenylphosphoranyliden)acetate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, acetic acid, water and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to an ether solvent which is more preferably tetrahydrofuran.

The reaction temperature is generally 0°C - 100°C , preferably 0°C - 70°C , and the reaction time is generally 15 min-12 hr, preferably 30 min-3 hr.

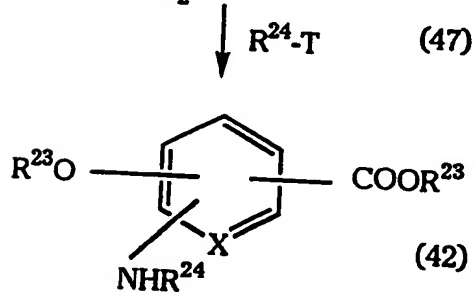
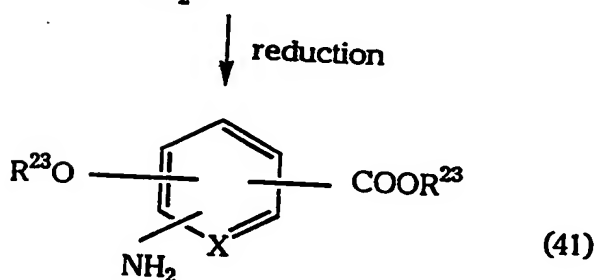
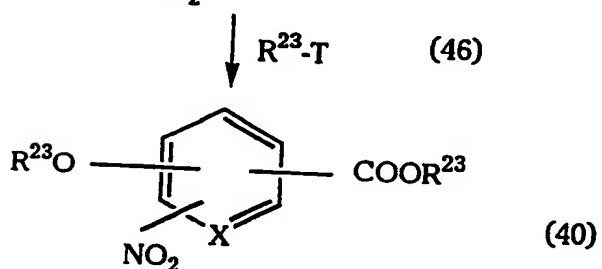
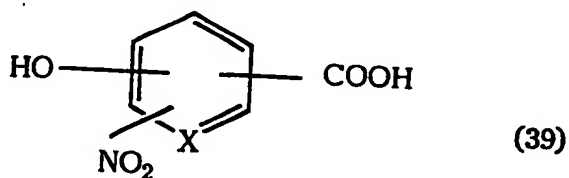
(2) Then, the Compound (36) obtained in (1) is hydrolyzed in the presence of a base to give Compound (37).

As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate,

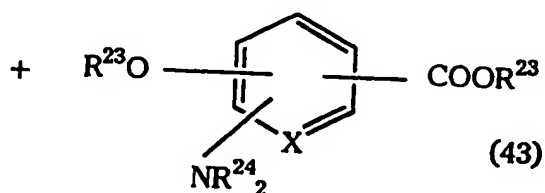
sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to lithium carbonate.

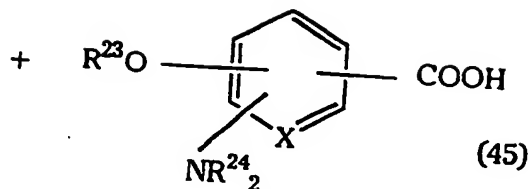
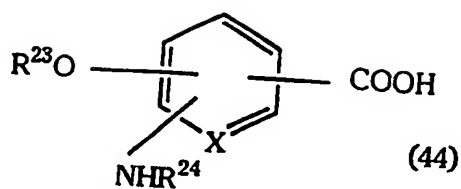
(3) The Compound (37) obtained in (2) is reacted in the same manner as in Production Method 1-A(3) and (4) to give Compound (38).

Production Method 1-C



↓ hydrolysis



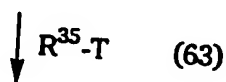
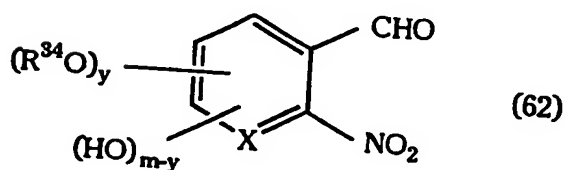
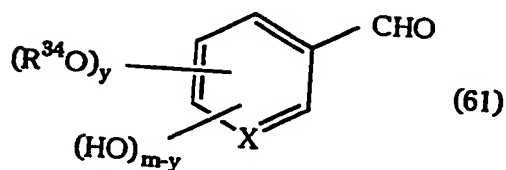
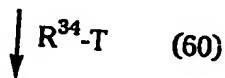
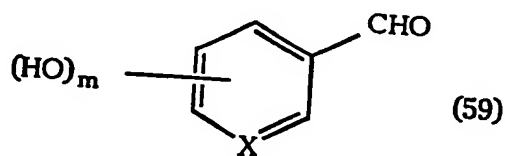


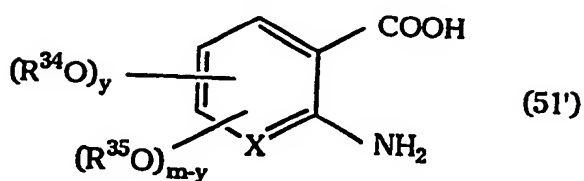
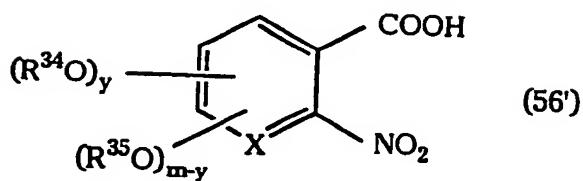
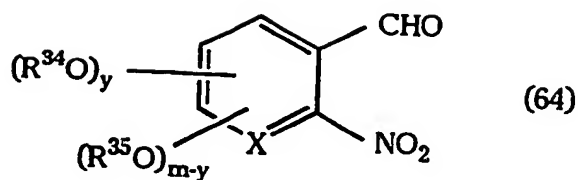
wherein R^{23} and R^{24} are each the same as those shown with regard to R^1 and other symbols are as defined above.

The Compound (39) is reacted with Compound (46) to give Compound (40). Then, Compound (40) is reduced by a conventional method to give Compound (41). Further, Compound (41) is reacted with Compound (47) to give Compound (42) and Compound (43). Then, Compound (42) and Compound (43) are hydrolyzed to give Compound (44) and Compound (45).

The reagent and conditions of the aforementioned reactions and the like are the same as those in Production Method 1-A.

Production Method 1-D





wherein R^{34} and R^{35} are respectively similar to those exemplified for R^1 and other symbols are as defined above.

(1) Using Compound (59) as a starting material, the hydroxy group is converted to ether with Compound (60) in the presence of a base to give Compound (61).

As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to lithium carbonate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropyl

alcohol, t-butanol and the like, with preference given to dimethylformamide.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 60°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(2) The Compound (61) is reacted with fuming nitric acid in the presence of conc. sulfuric acid to give Compound (62).

Examples of the solvent include ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like; and acid solvents such as acetic acid, acetic anhydride and the like, with preference given to acetic acid.

The reaction temperature is generally from -50°C to 200°C , preferably from -10°C to 60°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(3) The hydroxy group of Compound (62) is subjected to etherification with Compound (63) in the presence of a base to give Compound (64).

As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to potassium carbonate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to dimethylformamide.

The reaction temperature is generally from -10°C to 200°C , preferably 0°C - 60°C , and the reaction time is generally 15 min-48 hr, preferably 1-8 hr.

(4) The Compound (64) is oxidized to give Compound (56).

The oxidizing agent to be used is, for example, NaClO_2 , CrO_3 , $\text{K}_2\text{Cr}_2\text{O}_7$, KMnO_4 and the like.

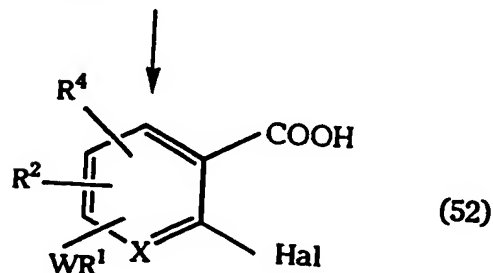
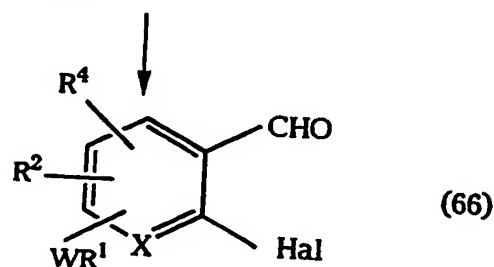
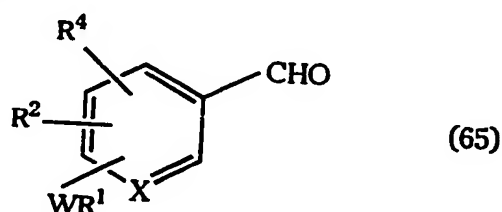
As an additive, for example, NaHPO_4 , KHPO_4 , amylene and the like may be used as appropriate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, acetic acid, water and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to isopropyl alcohol and t-butanol.

The reaction temperature is generally from 0°C to 100°C , preferably 0°C - 30°C , and the reaction time is 10 min-6 hr, preferably 15 min-3 hr.

(5) The Compound (56) is reduced to Compound (51) by a conventional method.

Production Method 1-E



wherein each symbol is as defined above.

(1) The Compound (65) obtained by the method of Production Methods 1-A - 1-D is reacted with a halogenizing agent in a suitable solvent or a mixed solvent to give Compound (66).

Examples of the suitable solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme, dioxane and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; and polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, water and the like, with preference given to halogen solvents and a mixed solvent of dioxane and water.

The halogenizing agent is exemplified by N-bromosuccinimide, bromine and the like.

The reaction temperature is generally from 0°C to 200°C, preferably 0°C - 60°C, and the reaction time is generally 15 min-24 hr, preferably 30 min-3 hr.

(2) The Compound (66) is oxidized in a conventional manner in a suitable solvent to give Compound (52).

The oxidizing agent to be used is, for example, NaClO_2 , CrO_3 , $\text{K}_2\text{Cr}_2\text{O}_7$, KMnO_4 and the like.

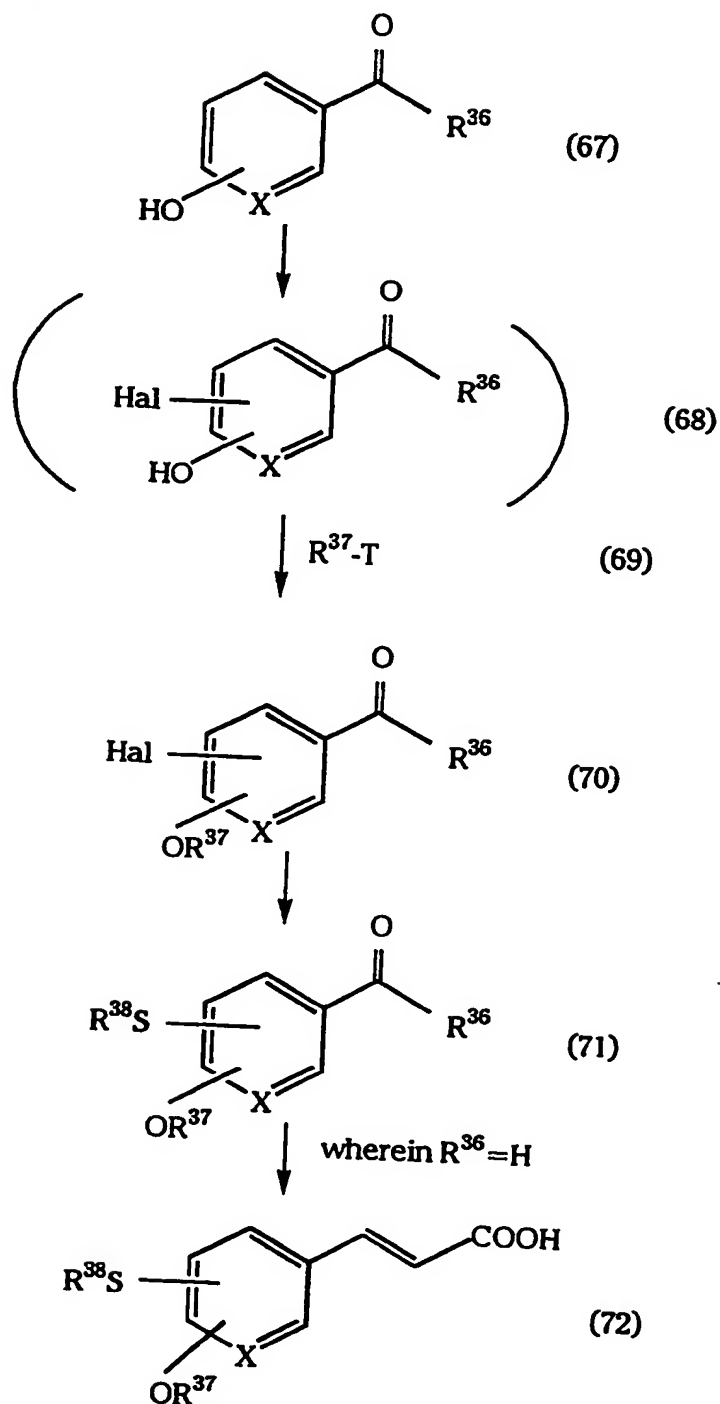
As an additive, NaHPO_4 , KHPO_4 , amylene and the like may be used as appropriate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, acetic acid, water and the like; and alcohol solvents such as methanol, ethanol, isopropyl alcohol, t-butanol and the like, with preference given to t-butanol.

The reaction temperature is generally from -30°C to 100°C, preferably 0°C -

30°C, and the reaction time is generally 10 min-12 hr, preferably 30 min-3 hr.

Production Method 1-F



wherein R^{36} is hydroxy or hydrogen atom, R^{37} is the same as R^1 and R^{38} is the same as R^2 .

In this method, alkylthio group is introduced onto the carbon adjacent to the carbon bearing substituent OH of Compound (67) to give Compound (71) or Compound (72).

For an improved reactivity of the carbon adjacent to the carbon bearing substituent OH, in the ring, the compound is halogenized to give Compound (68). A treatment of Compound (68) with a suitable base followed by addition of a suitable sulfur reagent affords a sulfide.

When converting to an alkylthio compound, the carboxyl group or carbonyl group of Compound (67) may be protected with oxazolidine, imidazolidine and the like by a conventional method. After the reaction, these protecting groups may be removed to regenerate the carboxyl group or carbonyl group by a conventional method.

(1) The Compound (67) is treated with a halogenizing agent in a suitable solvent to give Compound (68).

Examples of the halogenizing agent include bromine, N-bromosuccinimide, hydrogen bromide, hydrobromic acid, copper bromide and the like.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone, water and the like; and acid solvents such as acetic acid, hydrochloric acid, sulfuric acid and the like, with preference given to acetic acid.

The reaction temperature is generally from 0°C to 200°C, preferably 0°C - 60°C, and the reaction time is generally 10 min-18 hr, preferably 30 min-3 hr.

(2) Using Compound (68) and Compound (69), Compound (70) can be obtained in the same manner as in Production Method 1-A(1).

(3) The Compound (70) is treated with a sulfur agent in a suitable solvent in the presence of a base to give an alkylthio compound (71).

As the base, usable are, for example, LDA, n-butyllithium, s-butyllithium, t-butyllithium, LiHMDS, NaHMDS, KHMDS, sodium hydride, potassium hydride, EtMgBr, (i-Pr)₂NMgBr and the like, with preference given to n-butyllithium.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably tetrahydrofuran.

Examples of the sulfur agent include n-alkyldisulfide and the like.

Using this agent, the compound is converted to the n-alkyl(C₁-C₇)thio.

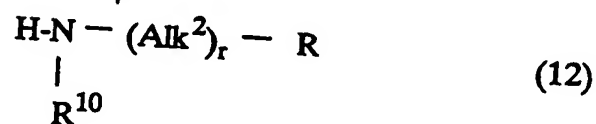
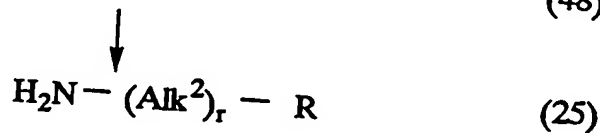
The reaction temperature is generally from -100°C to 50°C, preferably from -78°C to 30°C, and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(4) When Compound (71) is an aldehyde derivative wherein R³⁶ is hydrogen atom, aldehyde Compound (71) can be converted to Compound (72) in the same manner as in Production Method 1-B.

The Compound (11) having optional substituent(s) can be obtained by the above-mentioned Production Methods 1-A - 1-F.

Production Method 1-G

The Compound (12) to be used as a starting compound in Production Method 1 can be obtained, for example, as in the following.



wherein Alk^{2a} has one less carbons than Alk^2 and other symbols are as defined above.

(1) The Compound (48) is reduced with a suitable reducing agent to give Compound (25).

Examples of the reducing agent include BH_3 , $\text{BH}_3 \cdot \text{SMe}_2$, LiBH_4 , NaBH_4 , KBH_4 , NaBH_3OH , LiAlH_4 and the like, with preference given to LiAlH_4 .

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; and halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like, with preference given to an ether solvent which is more preferably tetrahydrofuran.

The reaction temperature is generally from -30°C to 100°C , preferably 0°C - 80°C , and the reaction time is generally 15 min-24 hr, preferably 1-6 hr.

(2) The Compound (25) obtained in (1) is reacted with Compound (49) in the presence of a base to give Compound (12).

As the base, usable are, for example, sodium carbonate, potassium carbonate, lithium carbonate, sodium hydrogencarbonate, potassium hydrogencarbonate, sodium hydroxide, potassium hydroxide, lithium hydroxide, sodium hydride, n-butyllithium, s-butyllithium, t-butyllithium, lithium diisopropylamide and the like, with preference given to potassium carbonate.

Examples of the solvent include hydrocarbon solvents such as benzene, toluene, hexane, xylene and the like; ether solvents such as diethyl ether, 1,2-dimethoxyethane, tetrahydrofuran, diglyme and the like; halogen solvents such as dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane and the like; ester solvents such as ethyl acetate, methyl acetate, butyl acetate and the like; polar solvents such as dimethylformamide, dimethyl sulfoxide, acetonitrile, acetone and the like; and alcohol solvents such as methanol, ethanol, isopropanol, t-butanol and the like, with preference given to dimethylformamide.

The reaction temperature is generally 0°C - 150°C , preferably 20°C - 100°C , and the reaction time is generally 1-48 hr, preferably 3-24 hr.

The Compound (I) produced as above can be separated and purified by a

known method such as concentration, concentration under reduced pressure, solvent extraction, crystallization, recrystallization, chromatography and the like.

The pharmaceutically acceptable salt of Compound (I) and various isomers of Compound (I) can be produced by a conventionally known method.

The Compound (I) and pharmaceutically acceptable salts thereof show pharmaceutical effects on mammals against the medical condition which is known to involve cannabinoid receptor, particularly, the medical condition in which peripheral cell tissues are involved (e.g., immune diseases, various inflammations, allergic diseases, nephritis and the like).

To be specific, the Compound (I) and pharmaceutically acceptable salts thereof selectively act on a cannabinoid receptor, particularly on peripheral receptors, cause less central side effects and have superior immunoregulating action, anti-inflammatory action, antiallergic action and therapeutic effect on nephritis.

Thus, the Compound (I) and pharmaceutically acceptable salts thereof are useful as cannabinoid receptor (particularly, peripheral cannabinoid receptor) activators and antagonists, immunoregulators, therapeutic agents for autoimmune diseases, antiinflammatory agents, antiallergic agents and therapeutic agents for nephritis.

When the Compound (I) and pharmaceutically acceptable salts thereof are used as pharmaceutical preparations, they are generally admixed with pharmacologically acceptable carriers, excipients, diluents, extenders, disintegrants, stabilizers, preservatives, buffering agents, emulsifiers, aromatics, colorants, sweeteners, thickeners, corrigents, solubilizers and other additives, all of which are known *per se*, such as water, vegetable oil, alcohols such as ethanol and benzyl alcohol, polyethylene glycol, glycerol triacetate, gelatin, lactose, carbohydrates such as starch and the like, magnesium stearate, talc, lanolin, petrolatum and the like and formulated by a conventional method into tablets, pills, powders, granules, suppositories, injections, eye drops, liquids, capsules, troches, aerosols, elixirs, suspensions, emulsions, syrups and the like, which can be administered orally or parenterally.

The dose varies depending on the kind of disease, severity thereof, the

compound to be administered, administration route, age, sex and body weight of patients, and the like. In the case of oral administration, the dose is generally 0.1 - 1,000 mg, preferably 1 - 300 mg of Compound (I) daily for an adult, which is administered in one to several doses.

The present invention is described in detail by illustrative Examples in the following, to which the present invention is not limited.

Preparative Example 1

4-Methoxytoluene (100 ml, 0.793 mol) and methylene chloride (300 ml) were mixed, and this solution was cooled to 0°C. To this solution was added aluminum chloride (190.3 g, 1.44 mol), and then heptanoyl chloride (123 ml, 0.8 mol) was added dropwise to this solution over 2 hours. The reaction mixture was heated to room temperature, and stirred for 2 hours. The reaction mixture was poured onto ice (400 g) to stop the reaction. The aqueous layer was extracted with chloroform (300 ml). The organic layers were combined, washed successively with water, a saturated aqueous sodium hydrogencarbonate solution and saturated brine (100 ml each), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated under reduced pressure, and the obtained residue was purified by distillation (120 pa, 125-140°C) to give 1-(2-hydroxy-5-methylphenyl)heptan-1-one (127.8 g, 77%) as a colorless oil.

¹H-NMR (CDCl₃) δ : 12.2(1H, s), 7.53(1H, s), 7.26(1H, d, J=8.47Hz), 6.88(1H, d, J=8.47Hz), 2.96(2H, t, J=7.31Hz), 1.79-1.67(2H, m), 1.47-1.25(6H, m), 0.90(3H, t, J=6.90Hz).

FABMS (m/z) : 235[M⁺H⁺] (10), 221(100), 202(40).

IR (Neat, cm⁻¹) : 3500-3100, 1642.

Preparative Example 2

1-(2-Hydroxy-5-methylphenyl)heptan-1-one (127 g, 0.61 mol), a 2.5N aqueous sodium hydroxide solution (250 ml) and ethanol (250 ml) were mixed, and this solution was cooled to 0°C. Dimethyl sulfate (60 ml) was added, and the mixture was refluxed under heating for 2 hours. Dimethyl sulfate (40 ml) and a 2.5N aqueous sodium hydroxide solution (170 ml) were further added, and the mixture was refluxed under heating for 2 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was extracted

twice with ether (200 ml). The organic layers were combined, washed twice with a 2.5N aqueous sodium hydroxide solution and saturated brine (100 ml each), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=95/5) to give 1-(2-methoxy-5-methylphenyl)heptan-1-one (82 g, 57%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.42(1H, s), 7.22(1H, d, $J=8.42\text{Hz}$), 6.83(1H, d, $J=8.42\text{Hz}$), 3.84(3H, s), 2.93(2H, t, $J=7.56\text{Hz}$), 2.28(3H, s), 1.70-1.59(2H, m), 1.45-1.20(6H, m), 0.87(3H, t, $J=6.2\text{Hz}$).

Preparative Example 3

1-(2-Methoxy-5-methylphenyl)heptan-1-one (81.6 g, 0.348 mol), ethyl chloroacetate (64 g, 0.522 mol) and benzene (100 ml) were mixed, and this solution was cooled to 0°C . Potassium t-butoxide (58.6 g, 0.522 mol) was added, and the mixture was stirred at room temperature for 0.5 hour. This solution was cooled again to 0°C . Then ethyl chloroacetate (32 g, 0.261 mol) and potassium t-butoxide (29.3 g, 0.261 mol) were added, and the mixture was stirred at room temperature for 0.5 hour. The reaction mixture was poured onto ice (200 g) to stop the reaction and the aqueous layer was extracted 3 times with toluene (120 ml). The organic layer was washed successively with water, an aqueous acetic acid solution (water/acetic acid=50/1) and water (100 ml each), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. To the obtained residue were added ethanol (90 ml) and sodium ethoxide previously prepared from sodium (13.1 g, 0.567 mol) and ethanol (260 ml), and the mixture was stirred at room temperature for 1.5 hours. Water (17 ml) was added to the reaction mixture, and the mixture was stirred for 0.5 hour. Ethanol was evaporated under reduced pressure. To this residue, water (350 ml) and conc. hydrochloric acid (63 ml) were added, and the mixture was refluxed under heating for 1.5 hours. The aqueous layer was extracted 3 times with ether (200 ml). The organic layers were combined, washed successively with water, a saturated aqueous sodium hydrogencarbonate solution and saturated brine (100 ml each), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated under reduced

pressure, and the obtained residue was distilled under reduced pressure (450 pa, 155-160°C) to give 2-(2-methoxy-5-methylphenyl)octanal (64.5 g, 74.6%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 9.65(1H, s), 7.06(1H, d, $J=8.32\text{Hz}$), 6.88(1H, s), 6.80(1H, d, $J=8.32\text{Hz}$), 3.79(3H, s), 3.74(2H, t, $J=8.46\text{Hz}$), 2.29(3H, s), 2.17-2.00(1H, m), 1.75-1.60(1H, m), 1.45-1.20(8H, m), 0.87(3H, t, $J=6.78\text{Hz}$).

FABMS (m/z) : 249 $[\text{M} + \text{H}^+]$ (80), 219(60).

Preparative Example 4

2-(2-Methoxy-5-methylphenyl)octanal (63.8 g, 0.257 mol), methyl iodide (160 ml, 2.57 mol) and benzene (300 ml) were mixed, and this solution was cooled to -5°C. Potassium t-butoxide (31.3 g, 0.279 mol) was added in such a manner that the temperature of the reaction mixture does not exceed 0°C, and the mixture was stirred at -2°C for 0.5 hour. The reaction mixture was poured into ice water (200 ml) to stop the reaction. The aqueous layer was extracted twice with ether (150 ml), and the organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Methanol (400 ml), an aqueous solution (110 ml) of semicarbazide hydrochloride (28.6 g, 0.257 mol) and pyridine (20.4 ml, 0.257 mol) were added to the obtained residue, and the mixture was stirred at room temperature for 0.75 hour. The precipitated crystals were collected by filtration, and washed with hexane. The crystals were dried to give 2-(2-methoxy-5-methylphenyl)octanal semicarbazide (64.7 g, 79%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.97(1H, s), 7.32(1H, s), 7.00(1H, s), 6.96(1H, d, $J=8.22\text{Hz}$), 6.73(1H, d, $J=8.22\text{Hz}$), 5.10(2H, bs), 3.71(3H, s), 2.26(3H, s), 2.08-1.93(1H, m), 1.84-1.72(1H, m), 1.42(3H, s), 1.28-0.9(8H, m), 0.82(3H, t, $J=6.66\text{Hz}$).

Preparative Example 5

2-(2-Methoxy-5-methylphenyl)octanal semicarbazide (64.7 g, 0.203 mol), potassium t-butoxide (47.8 g, 0.43 mol) and xylene (600 ml) were mixed, and this solution was refluxed under heating for 2.5 hours. This reaction mixture was

poured into ice water (200 ml) to stop the reaction. The aqueous layer was extracted 3 times with toluene (120 ml). The organic layer was washed 3 times with saturated brine (100 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (chloroform) to give 2-(1,1-dimethylheptyl)-1-methoxy-4-methylbenzene (51 g, overweight) as a mixture with xylene. The mixture was used for the next reaction. $^1\text{H-NMR}$ (CDCl_3) δ : 6.99(1H, s), 6.97(1H, d, $J=8.03\text{Hz}$), 6.75(1H, d, $J=8.03\text{Hz}$), 3.78(3H, s), 2.28(3H, s), 1.82-1.73(2H, m), 1.31(6H, s), 1.25-1.13(6H, m), 1.05-0.91(2H, m), 0.84(3H, t, $J=5.68\text{Hz}$).

Preparative Example 6

2-(1,1-Dimethylheptyl)-1-methoxy-4-methylbenzene (a mixture with xylene: calculated as 51 g, 0.203 mol), N-bromosuccinimide (38.4 g, 0.215 mol), benzoyl peroxide (0.97 g, 4 mmol) and carbon tetrachloride (500 ml) were mixed, and this solution was refluxed under heating for 3.5 hours. N-Bromosuccinimide (2.1 g, 12 mmol) was further added, and the mixture was refluxed under heating for 0.5 hour. N-Bromosuccinimide (36 g, 0.2 mol) was added, and this reaction mixture was refluxed under heating for 2 hours. The crystals were filtered off, and the mother liquor obtained was washed twice with saturated brine (100 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=20/1) to give 3-(1,1-dimethylheptyl)-4-methoxybenzaldehyde (33.4 g, 50% in 2 steps) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 9.87(1H, s), 7.77(1H, s), 7.74(1H, d, $J=8.32\text{Hz}$), 6.96(1H, d, $J=8.32\text{Hz}$), 3.91(3H, s), 1.83-1.70(2H, m), 1.37(6H, s), 1.35-1.06(6H, m), 1.04-0.85(2H, m), 0.83(3H, t, $J=6.74\text{Hz}$).
 FABMS (m/z) : 263 [$\text{M} + \text{H}^+$] (100), 247(95), 163(50).

Preparative Example 7

3-(1,1-Dimethylheptyl)-4-methoxybenzaldehyde (13 g, 49.5 mmol), t-butanol (65 ml) and 2-methyl-2-butene (35.2 ml, 332 mmol) were mixed, and to this

solution was added dropwise a solution prepared by mixing sodium chlorite (7.37 g, 64.4 mmol), sodium dihydrogenphosphate (7.73 g, 64.4 mmol) and water (50 ml). The mixture was stirred at room temperature for 12 hours. A 1N sodium hydroxide solution (100 ml) was added, and t-butanol was evaporated under reduced pressure. Conc. hydrochloric acid was added to make the mixture acidic. The aqueous layer was extracted 3 times with ethyl acetate (150 ml). The organic layers were combined, washed with saturated brine (100 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=5/1-2/1) to give 3-(1,1-dimethylheptyl)-4-methoxybenzoic acid (10.7 g, 77%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.98(1H, d, $J=2.15\text{Hz}$), 7.97(1H, dd, $J=9.12, 2.15\text{Hz}$), 6.89(1H, d, $J=9.12\text{Hz}$), 3.89(3H, s), 1.83-1.74(2H, m), 1.36(6H, s), 1.24-1.10(6H, m), 1.00-0.94(2H, m), 0.83(3H, t, $J=6.49\text{Hz}$).

FABMS (m/z) : 279 $[\text{M} + \text{H}^+]$ (65), 261(70), 193(100).

Preparative Example 8

3-(1,1-Dimethylheptyl)-4-methoxybenzaldehyde (1.5 g, 5.39 mmol), methanol (25 ml) and methyl (triphenylphosphoranylidene)acetate (3.24 g, 9.7 mmol) were mixed, and this solution was refluxed under heating for 7 hours. Saturated saturated brine was added to stop the reaction. The aqueous layer was extracted 3 times with ethyl acetate (10 ml). The organic layers were combined and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=20/1-10/1) to give methyl 3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]cinnamate (0.80 g, 47%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.65(1H, d, $J=16\text{Hz}$), 7.39(1H, s), 7.37(1H, d, $J=9.0\text{Hz}$), 6.85(1H, d, $J=9.0\text{Hz}$), 6.30(1H, d, $J=16\text{Hz}$), 3.85(3H, s), 3.79(3H, s), 1.84-1.73(2H, m), 1.34(6H, s), 1.28-1.12(6H, m), 1.01-0.85(2H, m), 0.83(3H, t, $J=6.45\text{Hz}$).

FABMS (m/z) : 319 $[\text{M} + \text{H}^+]$ (55), 287(65), 233(100).

Preparative Example 9

Methyl 3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]cinnamate (334.5 mg, 1.05 mmol), methanol (4 ml) and a 1N aqueous sodium hydroxide solution (1.2 ml, 1.2 mmol) were mixed, and this solution was refluxed under heating for 1 hour. Methanol was evaporated under reduced pressure. Conc. hydrochloric acid (0.3 ml) and saturated brine (5 ml) were added, and the aqueous layer was extracted 4 times with ethyl acetate (5 ml). The organic layers were combined, washed twice with saturated brine (5 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained crystals were washed with hexane to give 3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]cinnamic acid (0.33 g, quant.) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.75(1H, d, $J=15.9\text{Hz}$), 7.44-7.38(2H, m), 6.86(1H, d, $J=6.45\text{Hz}$), 6.32(1H, d, $J=15.9\text{Hz}$), 3.86(3H, s), 1.82-1.73(2H, m), 1.34(6H, s), 1.27-1.10(6H, m), 1.00-0.87(2H, m), 0.84(3H, t, $J=6.45\text{Hz}$).

Preparative Example 10

3-[3-(1,1-Dimethylheptyl)-4-methoxyphenyl]cinnamic acid (600 mg, 2.16 mmol) and methylene chloride (6 ml) were mixed in a reaction vessel replaced with nitrogen, and this solution was cooled to 0°C . To this solution was added dropwise a methylene chloride solution (4 ml) of boron tribromide (0.82 ml, 8.64 mmol), and the mixture was stirred at room temperature for 20 hours. A methylene chloride solution (5 ml) of boron tribromide (0.82 ml, 8.64 mmol) was further added dropwise, and the mixture was stirred at room temperature for 18 hours. This reaction mixture was poured into water (20 ml) to stop the reaction. Ether (20 ml) was added, and the organic layer was extracted 3 times with a 1N aqueous sodium hydroxide solution (20 ml). Conc. hydrochloric acid was added to make the mixture acidic. The aqueous layer was extracted 3 times with ethyl acetate (40 ml). The organic layers were combined, washed twice with saturated brine (20 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The residue obtained was purified by column chromatography (hexane/ethyl

acetate=6/1-1/2) to give 3-(1,1-dimethylheptyl)-4H-hydroxybenzoic acid (457 mg, 80%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.00(1H, s), 7.86(1H, d, $J=8.4\text{Hz}$), 6.72(1H, d, $J=8.4\text{Hz}$), 5.85-5.28(1H, bs), 1.87-1.77(2H, m), 1.40(6H, s), 1.30-1.14(6H, m), 1.07-0.93(2H, m), 0.83(3H, t, $J=6.8\text{Hz}$).
 FABMS (m/z) : 265 $[\text{M} + \text{H}^+]$ (100), 247(40), 179(60).

Preparative Example 11

Chromic acid (105.4 mg, 1.05 mmol, 1.2 eq) was dissolved in acetic acid (2 ml), and a solution of 3-(1,1-dimethylheptyl)benzaldehyde (205 mg, 0.878 mmol) in acetic acid (2 ml) was added to the solution under ice-cooling, which was followed by stirring for 2 minutes. The mixture was further stirred at room temperature for 30 minutes. Conc. sulfuric acid (2 drops) was added, and the mixture was stirred for 3 hours. To this reaction mixture, water (10 ml) was added, and the mixture was extracted twice with ethyl acetate (10 ml). The organic layers were combined, washed with saturated brine (20 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=2/1) to give 3-(1,1-dimethylheptyl)benzoic acid (205 mg, 99.0%).

$^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 8.08(1H, s), 7.92(1H, d, $J=7.7\text{Hz}$), 7.58(1H, d, $J=7.7\text{Hz}$), 7.39(1H, t, $J=7.7\text{Hz}$), 1.7-1.5(2H, m), 1.33(3H, s), 1.4-1.1(6H, m), 1.1-1.0(2H, m), 7.58(3H, t, $J=6.7\text{Hz}$).
 FABMS (m/z) : 249 $[\text{M} + \text{H}^+]$ (100), 163(80).
 IR (Neat, cm^{-1}) : 2927, 1689.

Preparative Example 12

2-Methyl-[1,4]-naphthoquinone (5 g, 29 mmol) and ether (200 ml) were mixed in a reaction vessel replaced with argon, and this solution was cooled to -10°C . A suspension (40 ml) of lithium aluminum hydride (1.0 g, 26.3 mmol) in ether was added dropwise to this solution over 40 minutes, and the mixture was stirred at room temperature for 0.5 hour. To the reaction mixture was added dropwise 1N hydrochloric acid (100 ml) to stop the reaction. The aqueous layer was extracted twice with ethyl acetate (100 ml). The organic layers were combined, washed

twice with saturated brine (50 ml), 3 times with a saturated aqueous sodium hydrogencarbonate solution (30 ml) and twice with saturated brine (50 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Water (10 ml) and conc. hydrochloric acid (10 ml) were added to the obtained residue, and the mixture was refluxed under heating for 2 hours. Water (50 ml) was added to this reaction mixture, and the aqueous layer was extracted twice with ether (50 ml). The organic layer was washed with water (30 ml), washed twice with a saturated aqueous sodium hydrogencarbonate solution (30 ml) and twice with saturated brine (30 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=30/1-10/1) to give 3-methylnaphthalen-1-ol in a mixture of compounds structurally unidentified. The mixture was not further purified, but used for the next reaction.

Preparative Example 13

The crude product of 3-methylnaphthalen-1-ol, dimethylformamide (DMF, 20 ml), potassium carbonate (3 g, 21.7 mmol) and pentyl bromide (4.0 ml, 32.3 mmol) were mixed in a reaction vessel replaced with argon, and this solution was stirred at 90°C for 3 hours. DMF was evaporated under reduced pressure, and water (20 ml) was added. The aqueous layer was extracted with ethyl acetate (20 ml) 3 times. The organic layer was washed with saturated brine (20 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=100/0-50/1) to give 3-methyl-1-pentyloxynaphthalene (827 mg, 12% in 3 steps) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.23(1H, d, $J=8.07\text{Hz}$), 7.69(1H, d, $J=8.07\text{Hz}$), 7.48-7.36(2H, m), 7.19(1H, s), 6.65(1H, s), 4.13(2H, t, $J=6.42\text{Hz}$), 2.49(3H, s), 1.98-1.87(2H, m), 1.53-1.37(4H, m), 0.98 (3H, t, $J=7.19\text{Hz}$).

Preparative Example 14

A crude product of 3-methyl-1-pentyloxynaphthalene, carbon tetrachloride

(15 ml) and N-bromosuccinimide (2.11 g, 11.9 mmol) were mixed. A solution (3 ml) of benzoyl peroxide (72.7 mg, 0.3 mmol) in carbon tetrachloride was added, and this solution was stirred at 100°C for 4 hours. The crystals were filtered off, and the mother liquor was washed twice with saturated brine (20 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=25/1) to give 1-bromo-2-dibromomethyl-4-pentyloxynaphthalene (1.16 g, 69%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.35-8.25(2H, m), 7.73-7.57(2H, m), 7.55(1H, s), 7.42(1H, s), 4.31(2H, t, $J=6.41\text{Hz}$), 2.10-1.97(2H, m), 1.82-1.45(4H, m), 1.04(3H, t, $J=7.19\text{Hz}$).

FABMS (m/z) : 466 [$\text{M}^+ \text{H}^+$] (20), 385(100), 315(40).

Preparative Example 15

1-Bromo-2-dibromomethyl-4-pentyloxynaphthalene (1.13 g, 2.43 mmol), acetic acid (8 ml) and sodium acetate (0.8 g, 9.72 mmol) were mixed, and this solution was refluxed under heating for 4 hours. Acetic acid was evaporated under reduced pressure. Water (5 ml) was added, and the aqueous layer was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (10 ml), a saturated aqueous sodium hydrogencarbonate solution (10 ml) and saturated brine (10 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=25/1) to give 1-bromo-4-pentyloxynaphthalene-2-carbaldehyde (0.647 g, 83%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 10.64(1H, s), 8.50-8.42(1H, m), 8.38-8.30(1H, m), 7.75-7.62(2H, m), 7.27(1H, s), 4.20(2H, t, $J=6.5\text{Hz}$), 2.00-1.88(2H, m), 1.60-1.36(4H, m), 0.97(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z) : 322 [$\text{M}^+ \text{H}^+$] (100), 251(65), 144(40).

Preparative Example 16

1-Bromo-4-pentyloxynaphthalene-2-carbaldehyde (0.77 g, 2.4 mmol), *t*-butanol (4.8 ml) and 2-methyl-2-butene (1.71 ml, 16.1 mmol) were mixed, and a

solution prepared by mixing sodium chlorite (360 mg, 3.12 mmol), sodium dihydrogenphosphate (374 mg, 3.12 mmol) and water (2.4 ml) was added dropwise. The mixture was stirred at room temperature for 16.5 hours. A 1N aqueous sodium hydroxide solution (5 ml) was added, and t-butanol was evaporated under reduced pressure. Conc. hydrochloric acid was added to make the mixture acidic. Saturated saturated brine (5 ml) was added, and the aqueous layer was extracted 3 times with ethyl acetate (10 ml). The organic layer was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure. The obtained residue was recrystallized from ethyl acetate to give 1-bromo-4-pentyloxynaphthalene-2-carboxylic acid (619 mg, 76%) as pale-yellow crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.47(1H, d, $J=8.4\text{Hz}$),
8.33(1H, d, $J=8.4\text{Hz}$), 7.72-7.58(2H, m), 7.24(1H, s),
4.18(2H, t, $J=6.48\text{Hz}$), 1.62-1.37(6H, m), 0.97(3H, t, $J=7.2\text{Hz}$).
FABMS (m/z) : 338 [$\text{M} + \text{H}^+$] (90), 339(70), 268(50).

Preparative Example 17

1-Bromo-4-pentyloxynaphthalene-2-carboxylic acid (400 mg, 1.19 mmol) and tetrahydrofuran (THF, 3 ml) were mixed in a reaction vessel replaced with argon, and this solution was cooled to -78°C . A hexane solution (1.6M, 1.63 ml) of n-butyllithium (2.61 mmol) was added, and the mixture was stirred for 1 hour. Water (0.5 ml) and saturated brine (2 ml) were added, and the aqueous layer was extracted 4 times with ethyl acetate (5 ml). The organic layers were combined and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=3/1-1/2) to give 4-pentyloxynaphthalene-2-carboxylic acid (149.6 mg, 49%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.32(1H, d, $J=7.47\text{Hz}$), 8.31(1H, s),
7.93(1H, d, $J=7.47\text{Hz}$), 7.68-7.52(2H, m), 7.42(1H, s),
4.23(2H, t, $J=6.48\text{Hz}$), 2.04-1.90(2H, m), 1.65-1.39(4H, m),
0.98(3H, t, $J=7.2\text{Hz}$).
FABMS (m/z) : 259 [$\text{M} + \text{H}^+$] (50), 258(100), 188(70).

Preparative Example 18

1-Bromo-4-pentyloxynaphthalene-2-carbaldehyde (0.644 g, 2.0 mmol), THF (5 ml) and methyl (triphenylphosphoranylidene)acetate (1.0 g, 3.0 mmol) were mixed, and this solution was refluxed under heating for 4 hours. THF was evaporated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=25/1) to give methyl 3-(1-bromo-4-pentyloxynaphthalen-2-yl)cinnamate (592 mg, 78%) as pale-yellow crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.38(1H, d, $J=15.9\text{Hz}$), 8.34(1H, d, $J=8.0\text{Hz}$), 8.27(1H, d, $J=8.0\text{Hz}$), 7.67-7.52(2H, m), 6.94(1H, s), 6.45(1H, d, $J=15.9\text{Hz}$), 4.15(2H, t, $J=6.44\text{Hz}$), 3.86(3H, s), 2.03-1.90(2H, m), 1.64-1.30(4H, m), 0.97(3H, t, $J=7.17\text{Hz}$).

FABMS (m/z) : 378 [$\text{M} + \text{H}^+$] (100), 379(60), 226(60).

Preparative Example 19

Methyl 3-(1-bromo-4-pentyloxynaphthalen-2-yl)cinnamate (588 mg, 1.56 mmol), ethanol (4 ml) and a 1N aqueous sodium hydroxide solution (4 ml) were mixed, and this solution was refluxed under heating for 1 hour. Ethanol was evaporated under reduced pressure and conc. hydrochloric acid was added to make the reaction mixture acidic. THF (5 ml) and ethyl acetate (20 ml) were added to dissolve the precipitated crystals. The organic layer was separated and the aqueous layer was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed 3 times with saturated brine (20 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by washing with hexane to give 3-(1-bromo-4-pentyloxynaphthalen-2-yl)cinnamic acid (540 mg, 95%) as pale-yellow crystals.

$^1\text{H-NMR}$ ($\text{DMSO}-d_6$) δ : 12.6(1H, bs), 8.26(1H, d, $J=7.76\text{Hz}$), 8.22(1H, d, $J=7.76\text{Hz}$), 7.03(2H, d, $J=8.4\text{Hz}$), 8.15(1H, d, $J=15.8\text{Hz}$), 7.75-7.60(2H, m), 7.34(1H, s), 6.84(1H, d, $J=15.8\text{Hz}$), 4.27(2H, t, $J=6.41\text{Hz}$), 1.93-1.80(2H, m), 1.59-1.33(4H, m), 0.93(3H, t, $J=7.15\text{Hz}$).

FABMS (m/z) : 364 [$\text{M} + \text{H}^+$] (20), 169(100).

Preparative Example 20

3-(1-Bromo-4-pentyloxynaphthalen-2-yl)cinnamic acid (100 mg, 0.275

mmol) and THF (2 ml) were mixed in a reaction vessel replaced with argon, and this solution was cooled to -78°C . A hexane solution (1.6M, 0.38 ml) of n-butyllithium (0.6 mmol) was added, and the mixture was stirred for 1 hour. Water (1 ml) and conc. hydrochloric acid were added to make this solution acidic ($\text{pH}=1$), and the aqueous layer was extracted 4 times with ethyl acetate (5 ml). The organic layers were combined, washed 3 times with saturated brine (5 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1) to give 3-(4-pentyloxynaphthalen-2-yl)cinnamic acid (46.2 mg, 59%) as colorless crystals.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 12.4(1H, bs), 8.16-8.10(1H, m), 7.91-7.86(1H, m), 7.71(1H, s), 7.69(1H, d, $J=15.9\text{Hz}$), 7.59-7.50(2H, m), 7.28(1H, s), 6.70(1H, d, $J=15.9\text{Hz}$), 4.23(2H, t, $J=6.42\text{Hz}$), 1.94-1.8(2H, m), 1.60-1.35(4H, m), 0.93(3H, t, $J=7.16\text{Hz}$).
 FABMS (m/z) : 285 $[\text{M} + \text{H}^+]$ (10), 284(300), 169(100).

Preparative Example 21

2-Hydroxy-3-methoxybenzoic acid (15.66 g, 93 mmol), DMF (200 ml), potassium carbonate (51.4 g, 372 mmol) and pentyl bromide (29 ml, 233 mmol) were mixed, and this solution was stirred at 90°C for 1 hour. DMF was evaporated under reduced pressure, and water (100 ml) was added. The aqueous layer was extracted 3 times with ethyl acetate (150 ml). The organic layers were combined, washed twice with saturated brine (70 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. To the obtained residue were added a 1N aqueous sodium hydroxide solution (70 ml) and ethanol (70 ml), and the mixture was refluxed under heating for 1 hour. A 1N aqueous sodium hydroxide solution (70 ml) and ethanol (70 ml) were further added, and the mixture was refluxed under heating for 2 hours. Ethanol was evaporated under reduced pressure, and conc. hydrochloric acid was added to make this solution acidic. The aqueous layer was extracted 3 times with ethyl acetate (100 ml). The organic layers were combined, washed twice with saturated brine (100 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was

concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1-1/1) to give 3-methoxy-2-pentyloxybenzoic acid (20.5 g, 97%) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.22(1H, d, $J=7.35\text{Hz}$), 7.20-7.09(2H, m), 4.26(2H, t, $J=6.96\text{Hz}$), 3.91(3H, s), 1.90-1.79(2H, m), 1.50-1.30(4H, m), 0.92(3H, t, $J=7.0\text{Hz}$).

Preparative Example 22

3-Methoxy-2-pentyloxybenzoic acid (1.5 g, 6.3 mmol), methanol (10 ml) and conc. sulfuric acid (1 drop) were mixed, and this solution was refluxed under heating for 7 hours. Methanol was evaporated under reduced pressure, and a saturated aqueous sodium hydrogencarbonate solution (3 ml) was added. The aqueous layer was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed twice with a saturated aqueous sodium hydrogencarbonate solution (5 ml) and once with saturated brine (5 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. THF (15 ml) was added to the obtained residue in a stream of argon, and the mixture was cooled to 0°C . Lithium aluminum hydride (0.49 g, 13 mmol) was added to this solution, and the mixture was stirred for 1 hour. Water (0.4 ml), a 1N aqueous sodium hydroxide solution (0.4 ml) and water (1.2 ml) were successively added dropwise to the reaction mixture. Ether (60 ml) was added, and the mixture was vigorously stirred for 1 hour. The inorganic salt was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of (3-methoxy-2-pentyloxyphenyl)methanol. The product was not further purified, and used in the next reaction.

Preparative Example 23

The crude product of (3-methoxy-2-pentyloxyphenyl)methanol (1.2 g), dimethyl sulfoxide (DMSO, 25 ml) and triethylamine (6.72 ml, 48.2 mmol) were mixed, and this solution was cooled to 0°C . Sulfur trioxide - pyridine complex (2.56 g, 16.1 mmol) was added, and the mixture was stirred at room temperature for 1 hour. The reaction mixture was poured into water to stop the reaction, and the aqueous layer was extracted 3 times with ethyl acetate (30 ml). The organic

layers were combined, washed with 2N hydrochloric acid (30 ml), water (30 ml) and saturated brine (30 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=15/1-10/1) to give 3-methoxy-2-pentyloxybenzaldehyde (1.16 g, 83% in 3 steps) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.42(1H, d, $J=6.69\text{Hz}$),
7.20-7.09(3H, m, involving a singlet at 7.13), 4.12(2H, t, $J=6.73\text{Hz}$),
3.89(3H, s), 1.90-1.75(2H, m), 1.52-1.32(4H, m), 0.93(3H, t, $J=7.08\text{Hz}$).
FABMS (m/z) : 223[$\text{M} + \text{H}^+$] (60), 164(20).

Preparative Example 24

3-Methoxy-2-pentyloxybenzaldehyde (1.15 g, 5.17 mmol), THF (20 ml) and methyl (triphenylphosphoranylidene)acetate (3.34 g, 10 mmol) were mixed, and this solution was refluxed under heating for 4 hours.

THF was evaporated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=3/1) to give methyl 3-(3-methoxy-2-pentyloxyphenyl)cinnamate (1.48 g, over weight) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.35(1H, d, $J=2.0\text{Hz}$),
7.15(1H, dd, $J=8.3, 2.0\text{Hz}$), 7.03(2H, d, $J=8.4\text{Hz}$),
6.80(2H, d, $J=8.4\text{Hz}$), 6.80(1H, d, $J=8.3\text{Hz}$), 6.62(1H, bs),
6.19(1H, t, $J=12.9\text{Hz}$), 3.98(2H, t, $J=6.9\text{Hz}$), 3.86(3H, s),
3.64(2H, q, $J=6.9\text{Hz}$), 2.82(2H, t, $J=6.9\text{Hz}$), 1.9-1.7(2H, m),
1.5-1.3(4H, m), 0.90(3H, t, $J=7.0\text{Hz}$).

FABMS (m/z) : 358[$\text{M} + \text{H}^+$] (100), 221(80), 154(60).

Preparative Example 25

Methyl 3-(3-methoxy-2-pentyloxyphenyl)cinnamate (1.47 g, 5.28 mmol), ethanol (10 ml) and a 1N aqueous sodium hydroxide solution (10 ml) were mixed, and this solution was refluxed under heating for 0.5 hour. Ethanol was evaporated under reduced pressure, and conc. hydrochloric acid was added to make the mixture acidic ($\text{pH}=1$). The precipitated crystals were extracted 3 times with ethyl acetate (20 ml). The organic layers were combined, washed 3 times with saturated brine (20 ml), and dried over anhydrous sodium sulfate. The

drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by recrystallization from ethanol to give 3-(3-methoxy-2-pentyloxyphenyl)cinnamic acid (1.09 g, 78%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.16(1H, d, $J=16.2\text{Hz}$), 7.19(1H, d, $J=7.99\text{Hz}$), 7.06(1H, d, $J=7.99\text{Hz}$), 6.95(1H, d, $J=7.99\text{Hz}$), 6.48(1H, d, $J=16.2\text{Hz}$), 3.99(2H, t, $J=6.88\text{Hz}$), 3.87(3H, s), 1.89-1.75(2H, m), 1.57-1.35(4H, m), 0.94(3H, t, $J=7.14\text{Hz}$).
 FABMS (m/z) : 265 $[\text{M} + \text{H}^+]$ (40), 264(70), 177(100).

Preparative Example 26

2-Hydroxy-3-methoxybenzoic acid (7.15 g, 30 mmol), toluene (60 ml), triethylamine (4.6 ml, 33 mmol) and diphenylphosphoryl azide (7.11 ml, 33 mmol) were mixed in a reaction vessel replaced with argon, and this solution was stirred at room temperature for 1 hour and then for 2.5 hours while heating from 45°C to 100°C . Benzyl alcohol (3.41 ml, 33 mmol) was added, and the mixture was refluxed under heating for 2 hours. To this reaction mixture was added ice water (60 ml) to stop the reaction, and the aqueous layer was extracted 3 times with ethyl acetate (50 ml). The organic layers were combined, washed twice with saturated brine (50 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=9/1) to give benzyl (3-methoxy-2-pentyloxyphenyl)carbamate (8.41 g, 82%) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.73(1H, d, $J=8.1\text{Hz}$), 7.42-7.31(6H, m), 7.01(1H, t, $J=8.4\text{Hz}$), 7.01(1H, d, $J=8.4\text{Hz}$), 5.21(2H, s), 3.99(2H, t, $J=6.8\text{Hz}$), 3.84(3H, s), 1.80-1.67(2H, m), 1.5-1.3(4H, m), 0.90(3H, t, $J=7.1\text{Hz}$).
 FABMS (m/z) : 344 $[\text{M} + \text{H}^+]$ (45), 343(100), 300(65).

Preparative Example 27

Benzyl (3-methoxy-2-pentyloxyphenyl)carbamate (2 g, 5.82 mmol), ethanol (50 ml) and 10% palladium-carbon catalyst (160 mg) were mixed, and this solution was stirred at room temperature for 4.5 hours in a stream of hydrogen. The

palladium-carbon catalyst was filtered off, and ethanol was evaporated under reduced pressure. Ethanol (10 ml) and diethyl ethoxymethylenemalonate (1.29 ml, 6.4 mmol) were added to the obtained residue, and this solution was refluxed under heating for 2 hours. Ethanol was evaporated under reduced pressure, and liquid paraffin (10 ml) was added to the obtained residue. The mixture was stirred at 250°C for 1 hour, and cooled to room temperature. A brown oil was separated from liquid paraffin, and ethyl acetate (3 ml) and hexane (10 ml) were added to this brown oil. The mixture was stirred and the obtained crystals were purified by washing with hexane and ether to give ethyl 7-methoxy-4-oxo-8-pentyloxy-1,4-dihydroquinoline-3-carboxylate (589 mg, 30% in 3 steps) as pale-brown crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 9.15(1H, bs), 8.55(1H, s), 8.12(1H, d, $J=9.1\text{Hz}$), 7.03(1H, d, $J=9.1\text{Hz}$), 4.36(2H, q, $J=7.1\text{Hz}$), 4.17(2H, t, $J=6.9\text{Hz}$), 3.96(3H, s), 1.85-1.69(2H, m), 1.50-1.32(7H, m), 0.91(3H, t, $J=7.0\text{Hz}$).

FABMS (m/z) : 334 [$\text{M} + \text{H}^+$] (100), 288(30), 218(20).

Preparative Example 28

Ethyl 7-methoxy-4-oxo-8-pentyloxy-1,4-dihydroquinoline-3-carboxylate (580 mg, 1.74 mmol) and phosphorus oxychloride (3 ml) were mixed, and this solution was refluxed under heating for 1 hour. This reaction mixture was poured onto ice (30 g) to stop the reaction. A 30% aqueous sodium hydroxide solution (20 ml) was gradually added dropwise under ice-cooling. The aqueous layer was extracted 4 times with ether (20 ml). The organic layers were combined, washed twice with saturated brine (10 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1) to give ethyl 4-chloro-7-methoxy-8-pentyloxyquinoline-3-carbamate (561 mg, 92%) as pale-yellow crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 9.21(1H, s), 8.16(1H, d, $J=9.0\text{Hz}$), 7.47(1H, d, $J=9.0\text{Hz}$), 4.48(2H, q, $J=7.2\text{Hz}$), 4.26(2H, t, $J=7.1\text{Hz}$), 4.05(3H, s), 1.94-1.74(2H, m), 1.51-1.30(7H, m), 0.92(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 352 [$\text{M} + \text{H}^+$] (100), 294(60).

Preparative Example 29

Ethyl 4-chloro-7-methoxy-8-pentyloxyquinoline-3-carbamate (311 mg, 0.84 mmol), ethanol (3 ml) and a 1N aqueous sodium hydroxide solution (3 ml) were mixed, and this solution was refluxed under heating for 0.5 hour. Ethanol was evaporated under reduced pressure, and conc. hydrochloric acid was added to make the reaction mixture acidic. THF (10 ml) and ethyl acetate (10 ml) were added to dissolve the precipitated crystals. The organic layer was separated, washed 3 times with saturated brine (10 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was recrystallized from ethanol to give 4-chloro-7-methoxy-8-pentyloxyquinoline-3-carbamic acid (229 mg, 80%) as pale-yellow crystals.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 13.8(1H, bs), 9.07(1H, s), 8.10(1H, d, $J=9.6\text{Hz}$), 7.75(1H, d, $J=9.6\text{Hz}$), 4.13(2H, t, $J=6.5\text{Hz}$), 3.99(3H, s), 1.78-1.67(2H, m), 1.50-1.28(4H, m), 0.88(3H, t, $J=7.4\text{Hz}$).
 FABMS (m/z) : 324 [$\text{M}^+ \text{H}^+$] (85), 307(25), 266(25).

Preparative Example 30

4-Chloro-7-methoxy-8-pentyloxyquinoline-3-carbamic acid (101 mg, 0.312 mmol) and methanol (10 ml) were mixed, and 10% palladium-carbon catalyst (30 mg) was added to this solution. The mixture was stirred at room temperature for 5 hours in a stream of hydrogen. The palladium-carbon catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=10/1-6/4) to give 7-methoxy-8-pentyloxyquinoline-3-carbamic acid (74.6 mg, 83%) as yellow crystals.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$) δ : 9.32(1H, s), 8.70(1H, s), 7.80(1H, d, $J=4.52\text{Hz}$), 7.54(1H, d, $J=4.52\text{Hz}$), 4.16(2H, t, $J=6.53\text{Hz}$), 3.95(3H, s), 1.83-1.68(2H, m), 1.57-1.30(4H, m), 0.90(3H, t, $J=7.18\text{Hz}$).
 FABMS (m/z) : 290 [$\text{M}^+ \text{H}^+$] (100), 258(35), 220(60).

Preparative Example 31

3-Bromo-4-methoxybenzaldehyde (15 g, 70 mmol), t-butanol (140 ml), 2-methyl-2-butene (50 ml, 469 mmol) were mixed, and to this solution was added dropwise a solution prepared by mixing sodium chlorite (10.42 g, 91 mmol),

sodium dihydrogenphosphate dihydrate (14.2 g, 91 mmol) and water (70 ml). The mixture was stirred at room temperature for 16 hours. A 1N aqueous sodium hydroxide solution (50 ml) was added, and t-butanol was evaporated under reduced pressure. Conc. hydrochloric acid was added to make the mixture acidic. The precipitated crystals were collected by filtration and washed with hexane. The obtained crystals were dissolved in ethyl acetate (200 ml), and this solution was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 3-bromo-4-methoxybenzoic acid (10.5 g, 65%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 12.9(1H, bs), 8.06(1H, s), 7.94(1H, d, $J=8.5\text{Hz}$), 7.20(1H, d, $J=8.5\text{Hz}$), 3.93(3H, s).
 FABMS (m/z) : 232 [$\text{M} + \text{H}^+$] (800), 233(90), 231(100).

Preparative Example 32

3-Bromo-4-methoxybenzoic acid (8.75 g, 37.9 mmol), toluene (80 ml), ethyl acetate (20 ml), methylene chloride (20 ml) and DMF (1 drop) were mixed, and to this solution was added thionyl chloride (6.5 ml, 90 mmol). The mixture was stirred at 70°C for 0.5 hour. The reaction mixture was concentrated under reduced pressure, and toluene was added. The mixture was further concentrated under reduced pressure. Methylene chloride (160 ml) was added to the obtained residue, and this solution was cooled to 0°C. 2-Amino-2-methyl-1-propanol (7.64 ml, 80 mmol) was added dropwise, and the mixture was stirred at room temperature for 14 hours. The precipitated crystals were filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was diluted with ethyl acetate (200 ml), and this solution was washed with 1N hydrochloric acid (50 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure. The obtained residue and methylene chloride (150 ml) were mixed, and thionyl chloride (10.9 ml, 150 mmol) was added under ice-cooling. The mixture was stirred at room temperature for 2 hours. To this reaction mixture were successively added water (13 ml) and a 50% aqueous sodium hydroxide solution (40 ml) under ice-cooling. The aqueous layer was extracted 3 times with ethyl acetate (100 ml). The organic layers were combined, washed

twice with saturated brine (100 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1-1/2) to give 2-(3-bromo-4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (7.10 g, 66%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.15(1H, s), 7.85(1H, d, $J=8.5\text{Hz}$), 6.90(1H, d, $J=8.5\text{Hz}$), 4.09(2H, s), 3.93(3H, s), 1.37(6H, s).

FABMS (m/z) : 285 $[\text{M} + \text{H}^+]$ (200), 286(90), 284(100).

Preparative Example 33

2-(3-Bromo-4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (2.1 g, 7.4 mmol) and THF (15 ml) were mixed, and this solution was cooled to -78°C . A hexane solution (1.6M, 4.75 ml) of *n*-butyllithium (7.6 mmol) was added, and the mixture was stirred for 2 hours. DMF (1.16 ml, 15 mmol) was added and the mixture was stirred for 20 minutes. Water (20 ml) was added to stop the reaction. The aqueous layer was extracted twice with ethyl acetate (20 ml). The organic layers were combined, and washed with saturated brine (30 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=3/1-1/3) to give 5-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-methoxybenzaldehyde (0.71 g, 41%) as colorless transparent crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.36(1H, d, $J=2.3\text{Hz}$), 8.15(1H, dd, $J=8.8, 2.3\text{Hz}$), 7.01(1H, d, $J=8.8\text{Hz}$), 4.09(2H, s), 3.97(3H, s), 1.37(6H, s).

Preparative Example 34

Pentyltriphenylphosphonium bromide (1.17 g, 2.83 mmol) and ether (5 ml) were mixed, and to this solution was added a hexane solution (1.6M, 1.77 ml) of *n*-butyllithium (2.83 mmol). The mixture was stirred at room temperature for 2 hours. A THF solution (3 ml) of 5-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-methoxybenzaldehyde (600.8 mg, 2.58 mmol) was added to this solution, and the mixture was stirred for 1.5 hours. Water (5 ml) was added to stop the reaction. The aqueous layer was extracted 3 times with ethyl acetate (5 ml). The organic

layers were combined, and washed twice with saturated brine (20 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1) to give 2-[3-(1-hexenyl)-4-methoxyphenyl]-4,4-dimethyl-4,5-dihydrooxazole (583.3 mg, 79%) as a mixture (a colorless oil) of geometrical isomers (1:1).

¹H-NMR (CDCl₃)

E-isomer

δ: 7.99(1H, s), 7.75(1H, d, J=8.4Hz), 6.87(1H, d, J=8.4Hz), 6.66(1H, d, J=15.9Hz), 6.32(1H, dt, J=15.9, 6.9Hz), 4.08(2H, s), 3.87(3H, s), 2.28-2.18(2H, m), 1.51-1.26(10H, m, involving a singlet at 1.37), 0.87(3H, t, J=7.2Hz).

Z-isomer

δ: 7.83(1H, d, J=8.4Hz), 7.77(1H, s), 6.84(1H, d, J=8.4Hz), 6.44(1H, d, J=11.7Hz), 5.75(1H, dt, J=11.7, 7.26Hz), 4.08(2H, s), 3.86(3H, s), 2.30-2.21(2H, m), 1.51-1.30(4H, m), 0.92(3H, t, J=7.5Hz).

Preparative Example 35

6N Hydrochloric acid (20 ml) was added to 2-[3-(1-hexenyl)-4-methoxyphenyl]-4,4-dimethyl-4,5-dihydrooxazole (583 mg, 2.03 mmol), and the mixture was refluxed under heating for 4 hours. Saturated saturated brine (30 ml) was added to this solution, and the aqueous layer was extracted 3 times with ethyl acetate (50 ml). The organic layers were combined, and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=2/1) to give 3-(1-hexenyl)-4-methoxybenzoic acid (164.3 mg, 35%) as a mixture (colorless crystals) of geometrical isomers (1:1).

¹H-NMR (CDCl₃)

E-isomer

δ: 8.17(1H, d, J=2.13Hz), 7.95(1H, dd, J=8.31, 2.13Hz), 6.92(1H, d, J=8.31Hz), 6.67(1H, d, J=16.0Hz),

6.32(1H, dt, $J=16.0, 6.95\text{Hz}$), 3.92(3H, s), 2.30-2.21(2H, m),
1.51-1.30(4H, m), 0.89(3H, t, $J=7.18\text{Hz}$).

Z-isomer

δ : 8.02(1H, dd, $J=8.66, 2.18\text{Hz}$), 8.00(1H, d, $J=2.13\text{Hz}$),
6.89(1H, d, $J=8.66\text{Hz}$), 6.47(1H, d, $J=11.6\text{Hz}$),
5.79(1H, dt, $J=11.6, 7.36\text{Hz}$), 3.91(3H, s), 2.30-2.21(2H, m),
1.51-1.30(4H, m), 0.93(3H, t, $J=7.28\text{Hz}$).

Preparative Example 36

3-(1-Hexenyl)-4-methoxybenzoic acid (160 mg, 0.683 mmol) and ethanol (7 ml) were mixed, and to this solution was added 10% palladium-carbon catalyst (30 mg). The mixture was stirred at room temperature for 3 hours in a stream of hydrogen. The palladium-carbon catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by washing with hexane to give 3-hexyl-4-methoxybenzoic acid (116 mg, 72%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.97(1H, d, $J=8.63\text{Hz}$), 7.88(1H, s),
6.88(1H, d, $J=8.63\text{Hz}$), 3.89(3H, s), 2.63(2H, t, $J=7.72\text{Hz}$),
1.67-1.50(2H, m), 1.42-1.21(6H, m), 0.89(3H, t, $J=6.88\text{Hz}$).
FABMS (m/z): 237 [$\text{M} + \text{H}^+$] (100), 236(90), 219(80).

Preparative Example 37

A crude product of 3-hexyl-4-methoxybenzoic acid and methanol (4 ml) were mixed. To this solution was added conc. sulfuric acid (2 drops), and the mixture was refluxed under heating for 20 hours. Water (10 ml) was added and methanol was evaporated under reduced pressure. The aqueous layer was extracted 3 times with ethyl acetate (20 ml). The organic layers were combined, and washed 3 times with saturated brine (20 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=10/1) to give methyl 3-hexyl-4-methoxybenzoate (96.2 g) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.88(1H, dd, $J=8.55, 2.20\text{Hz}$),
7.82(1H, d, $J=2.20\text{Hz}$), 6.84(1H, d, $J=8.55\text{Hz}$), 3.90(3H, s), 3.87(3H, s),

2.61(2H, t, $J=7.74\text{Hz}$), 1.65-1.50(2H, m), 1.42-1.24(4H, m),
0.88(3H, t, $J=6.89\text{Hz}$).

FABMS (m/z): 251 $[M + H^+]$ (100), 219(45), 179(45).

Preparative Example 38

Methyl 3-hexyl-4-methoxybenzoate (93.2 mg, 0.372 mmol) and THF (2 ml) were mixed in a stream of argon. To this solution was added LAH (19 mg, 0.5 mmol) under ice-cooling, and the mixture was stirred for 1 hour. To this reaction mixture were successively added dropwise water (0.019 ml), a 1N aqueous sodium hydroxide solution (0.019 ml) and water (0.06 ml). Ether (20 ml) was added, and the mixture was vigorously stirred for 1 hour. The inorganic salt was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of (3-hexyl-4-methoxyphenyl)methanol. The obtained product was not further purified, and used in the next reaction.

Preparative Example 39

A crude product of (3-hexyl-4-methoxyphenyl)methanol, dimethyl sulfoxide (DMSO, 1.5 ml) and triethylamine (0.46 ml, 3.3 mmol) were mixed in a stream of argon. To this solution was added sulfur trioxide-pyridine complex (159 mg, 1 mmol) under ice-cooling, and the mixture was stirred at room temperature for 1 hour. This reaction mixture was poured into water (20 ml) to stop the reaction. The aqueous layer was extracted 3 times with ethyl acetate (20 ml). The organic layer was washed successively with 2N hydrochloric acid (20 ml), water (20 ml) and saturated brine (30 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=10/1) to give 3-hexyl-4-methoxybenzaldehyde (75.4 mg, 92% in 2 steps) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 9.87(1H, s), 7.72(1H, d, $J=8.1\text{Hz}$),
7.69(1H, s), 6.94(1H, d, $J=8.1\text{Hz}$), 3.91(3H, s), 2.64(2H, t, $J=7.7\text{Hz}$),
1.70-1.46(2H, m), 1.42-1.23(6H, m), 0.89(3H, t, $J=6.9\text{Hz}$).

FABMS (m/z): 221 $[M + H^+]$ (100), 149(30).

Preparative Example 40

3-Hexyl-4-methoxybenzaldehyde (70 mg, 0.318 mmol), THF (1.5 ml) and

methyl (triphenylphosphoranylidene)acetate (201 mg, 0.6 mmol) were mixed, and this solution was refluxed under heating for 5 hours. THF was evaporated under reduced pressure, and the obtained residue was purified by column chromatography (hexane/ethyl acetate=10/1) to give methyl 3-(3-hexyl-4-methoxyphenyl)cinnamate (84 mg, 96%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.64(1H, d, $J=15.6\text{Hz}$), 7.34(1H, d, $J=8.4\text{Hz}$), 7.32(1H, s), 6.93(1H, d, $J=8.4\text{Hz}$), 6.30(1H, d, $J=15.6\text{Hz}$), 3.85(3H, s), 3.79(3H, s), 2.59(2H, t, $J=7.7\text{Hz}$), 1.64-1.50(2H, m), 1.42-1.21(6H, m), 0.97-0.83(3H, m).
 FABMS (m/z) : 277 [$\text{M} + \text{H}^+$] (60), 276(100), 245(60).

Preparative Example 41

Methyl 3-(3-hexyl-4-methoxyphenyl)cinnamate (80 mg, 0.29 mmol), ethanol (1 ml) and a 1N aqueous sodium hydroxide solution (1 ml) were mixed, and this solution was refluxed under heating for 1.5 hours. Ethanol was evaporated under reduced pressure, and conc. hydrochloric acid was added to make the solution acidic. Ethyl acetate (5 ml) was added to dissolve the precipitated crystals. The organic layer was separated, and the aqueous layer was extracted twice with ethyl acetate (5 ml). The organic layers were combined, washed 3 times with saturated brine (8 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was recrystallized from ethyl acetate to give 3-(3-hexyl-4-methoxyphenyl)cinnamic acid (58 mg, 76%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.73(1H, d, $J=15.9\text{Hz}$), 7.37(1H, d, $J=8.1\text{Hz}$), 7.35(1H, s), 6.84(1H, d, $J=8.1\text{Hz}$), 6.56(1H, d, $J=15.9\text{Hz}$), 2.60(2H, t, $J=8.0\text{Hz}$), 1.73-1.50(2H, m), 1.43-1.22(6H, m), 0.89(3H, t, $J=6.6\text{Hz}$).
 FABMS (m/z) : 263 [$\text{M} + \text{H}^+$] (60), 262(100), 191(40).

Preparative Example 42

Bromoacetyl bromide (7.73 g, 0.0383 mol, 1.0 eq) was dissolved in carbon disulfide (35 ml), and the solution was cooled with an ice salt. Anhydrous aluminum chloride (10.2 g, 0.077 mol, 2.0 eq) and 2-pentyloxyphenol (6.9 g, 0.0383 mol, 1.0 eq) were successively added, and the mixture was stirred for 1

hour. The mixture was further stirred at room temperature for 4 hours, and water (10 ml) and dilute hydrochloric acid (10 ml) were carefully added under ice-cooling. The reaction mixture was extracted twice with ether (10 ml). The organic layers were combined, washed with saturated brine (30 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=5/1) to give 1-(4-hydroxy-3-pentyloxyphenyl)-2-bromoethanone (6.58 g, 57.0%).

$^1\text{H-NMR}$ (CDCl_3) δ : 7.55(1H, d, $J=8.1\text{Hz}$), 7.54(1H, s), 6.97(2H, d, $J=8.1\text{Hz}$), 6.19(1H, s), 4.40(2H, s), 4.12(2H, t, $J=6.6\text{Hz}$), 1.9-1.8(2H, m), 1.5-1.4(4H, m), 0.94(3H, t, $J=7.0\text{Hz}$).

FABMS (m/z) : 302 [$\text{M}^+ \text{H}^+$] (80), 301(85).

Preparative Example 43

A solution of sodium hydroxide (680 mg), water (2 ml) and antiformin (34 ml) was heated to 55°C. 1-(4-Hydroxy-3-pentyloxyphenyl)-2-bromoethanone (3.01 g, 0.01 mol, 1.0 eq) was added, and the mixture was stirred at 60°C-70°C for 40 minutes. An aqueous solution (10 ml) of sodium thiosulfate (1.2 g) was added, and the mixture was cooled to room temperature. Conc. hydrochloric acid (5 ml) was added to adjust the mixture to pH 5-6. Water (50 ml) was added to this reaction mixture, and the mixture was extracted twice with ethyl acetate (100 ml). The organic layers were combined, washed with saturated brine (200 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate/acetic acid=2/1/0.01) to give 4-hydroxy-3-pentyloxybenzoic acid (1.24 g, 55.3%).

$^1\text{H-NMR}$ (CDCl_3) δ : 8.0-6.8(3H, m), 6.3(1H, bs), 4.2-4.0(2H, m), 2.0-1.8(2H, m), 1.6-1.4(4H, m), 0.9(3H, t, $J=7.5\text{Hz}$).

FABMS (m/z) : 225 [$\text{M}^+ \text{H}^+$] (80), 207(50).

Preparative Example 44

3-Hydroxy-4-methoxybenzoic acid (9.6 g, 0.057 mol) was dissolved in DMF (90 ml), and to this solution were successively added 1-bromopentane (25.9 g, 0.17 mol, 3.0 eq) and anhydrous potassium carbonate (47.4 g, 0.34 mol, 6.0 eq). The

mixture was stirred under heating at 90°C for 3 hours. This reaction mixture was cooled to room temperature, and anhydrous potassium carbonate was filtered off. Water (200 ml) was added to the filtrate, and the mixture was extracted twice with ethyl acetate (200 ml). The organic layers were combined, washed with saturated brine (300 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=15/1-10/1) to give pentyl 4-methoxy-3-pentyloxybenzoate (17.4 g, 98.8%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.7(1H, dd, $J=9$, 3Hz),
7.6(1H, d, $J=3\text{Hz}$), 6.9(1H, d, $J=9\text{Hz}$), 4.3(2H, t, $J=9\text{Hz}$),
4.1(2H, t, $J=8\text{Hz}$), 3.9(3H, s), 2.0-1.7(4H, m), 1.5-1.3(8H, m),
0.9(6H, t, $J=8.0\text{Hz}$).

FABMS (m/z) : 309[$\text{M} + \text{H}^+$] (80), 308(100), 239(42).

IR (Neat, cm^{-1}) : 2956, 1712.

Elemental analysis : $\text{C}_{18}\text{H}_{28}\text{O}_4$

Calculated C 70.10, H 9.15

Found C 70.19, H 9.25

Preparative Example 45

Pentyl 4-methoxy-3-pentyloxybenzoate (17.4 g, 0.056 mol) was dissolved in methanol (85 ml). A 1N aqueous sodium hydroxide solution (85 ml, 0.085 mol, 1.5 eq) was added, and the mixture was refluxed under heating for 1.5 hours. This reaction mixture was cooled to room temperature, and washed with n-hexane (100 ml). A 10% aqueous hydrochloric acid solution (ca. 120 ml) was added to the aqueous layer under ice-cooling to make the same acidic. This was extracted twice with ethyl acetate (220 ml). The organic layers were combined, washed with saturated brine (400 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by recrystallization from ethyl acetate to give 4-methoxy-3-pentyloxybenzoic acid (10.7 g, 79.6%) as colorless crystals.

m.p. : 124.6-125.0°C

$^1\text{H-NMR}$ (CDCl_3) δ : 7.76(1H, d, $J=2.1\text{Hz}$),

7.60(1H, dd, $J=8.6, 2.1\text{Hz}$), 6.92(1H, d, $J=8.6\text{Hz}$), 4.08(2H, t, $J=7.0\text{Hz}$),
4.05(3H, s), 2.1-1.8(2H, m), 1.6-1.3(4H, m), 0.94(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z): 239 [$M + H^+$] (80), 238(100), 168(57).

IR (KBr, cm^{-1}): 3432, 2951, 1678.

Elemental analysis: $\text{C}_{13}\text{H}_{18}\text{O}_4$

Calculated C 65.53, H 7.61

Found C 65.65, H 7.74

Preparative Example 46

3-Hydroxy-4-methoxycinnamic acid (9.7 g, 0.050 mol, 1.0 eq) was dissolved in DMF (90 ml). 1-Bromopentane (22.7 g, 0.150 mol, 3.0 eq) and anhydrous potassium carbonate (41.5 g, 0.30 mol, 6.0 eq) were successively added to this solution, and the mixture was stirred under heating at 90°C for 3 hours. This reaction mixture was cooled to room temperature, and anhydrous potassium carbonate was filtered off. Water (200 ml) was added to the filtrate, and the mixture was extracted twice with ethyl acetate (200 ml). The organic layers were combined, washed with saturated brine (300 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=15/1-10/1) to give pentyl 4-methoxy-3-pentyloxycinnamate (18.2 g, 100%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.62(1H, d, $J=15.0\text{Hz}$),

7.08(1H, dd, $J=10.3, 1.9\text{Hz}$), 7.06(1H, d, $J=1.9\text{Hz}$),

6.86(1H, d, $J=10.3\text{Hz}$), 6.30(1H, d, $J=15.0\text{Hz}$), 4.19(2H, t, $J=9.0\text{Hz}$),

4.03(2H, t, $J=6.0\text{Hz}$), 3.89(3H, s), 1.9-1.6(4H, m), 1.5-1.3(8H, m),
1.0-0.9(6H, m).

FABMS (m/z): 335 [$M + H^+$] (55), 334(100), 247(62).

IR (Neat, cm^{-1}): 2954, 1710.

Elemental analysis: $\text{C}_{20}\text{H}_{30}\text{O}_4$

Calculated C 71.82, H 9.04

Found C 71.99, H 9.28

Preparative Example 47

Pentyl 4-methoxy-3-pentyloxycinnamate (18.0 g, 0.050 mol) was dissolved in

methanol (75 ml). A 1N aqueous sodium hydroxide solution (75 ml, 0.075 mol, 1.5 eq) was added, and the mixture was refluxed under heating for 1 hour. This reaction mixture was cooled to room temperature, and a 10% aqueous hydrochloric acid solution (ca. 100 ml) was added under ice-cooling to make the mixture acidic. This was extracted twice with ethyl acetate (150 ml). The organic layers were combined, washed with saturated brine (300 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by recrystallization from ethyl acetate to give 4-methoxy-3-pentyloxycinnamic acid (12.2 g, 93%) as colorless crystals.

m.p. : 150.0-150.3°C

$^1\text{H-NMR}$ (CDCl_3) δ : 7.73(1H, d, $J=16.0\text{Hz}$),
7.13(1H, dd, $J=8.1, 1.9\text{Hz}$), 7.09(1H, d, $J=1.9\text{Hz}$), 6.88(1H, d, $J=8.1\text{Hz}$),
6.31(1H, d, $J=16.0\text{Hz}$), 4.04(2H, t, $J=6.8\text{Hz}$), 3.91(3H, s),
2.1-1.8(2H, m), 1.5-1.3(4H, m), 0.94(3H, t, $J=7.0\text{Hz}$).

FABMS (m/z) : 265 [$\text{M} + \text{H}^+$] (62), 264(100), 247(40).

IR (KBr , cm^{-1}) : 2934, 1679.

Elemental analysis : $\text{C}_{15}\text{H}_{20}\text{O}_4$

Calculated C 68.16, H 7.63

Found C 68.20, H 7.78

Preparative Example 48

3,4-Dihydroxybenzoic acid (462 mg, 3 mmol) was dissolved in DMF (10 ml). Potassium carbonate (3.73 g, 27 mmol, 9 eq) and 1-bromopentane (1.70 ml, 13.5 mmol, 4.5 eq) were successively added to this solution at room temperature, and the mixture was stirred at 110°C for 24 hours. This reaction mixture was filtered, and the residual potassium carbonate was washed with ethyl acetate (50 ml). The filtrate was washed with water (15 ml x 3) and saturated brine (15 ml). The organic layer was dried over anhydrous sodium sulfate. After the drying agent was filtered off, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=95/5) to give pentyl 3,4-dipentyloxybenzoate (912 mg, 83%).

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 7.66(1H, d, $J=8.4, 1.9\text{Hz}$),

7.57(1H, d, J=1.9Hz), 6.89(1H, d, J=8.4Hz), 4.31(2H, t, J=6.7Hz),
4.07(4H, 2t, J=6.6Hz), 1.90-1.76(6H, m), 1.52-1.38(12H, m),
0.98-0.94(9H, m).

FABMS (+) (m/z) : 465[M + 1] (61),
364[M](100), 295(45), 276(42).

Preparative Example 49

Pentyl 3,4-dipentyloxybenzoate (911 mg, 2.50 mmol) was dissolved in methanol (15.0 ml). To this solution was added a 1N aqueous potassium hydroxide solution (7.5 ml, 7.5 mmol, 3 eq), and the mixture was stirred with reflux for 5 hours. A 3N aqueous hydrochloric acid solution was added to this reaction mixture to make the same acidic (pH <2). The mixture was extracted with chloroform (20 ml x 3). The organic layer was washed with saturated brine (20 ml). The organic layer was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure to give a colorless solid. This was recrystallized from ethyl acetate-hexane to give 3,4-dipentyloxybenzoic acid (512 mg, 70%) as colorless crystals.

¹H-NMR (CDCl₃, 300MHz) δ : 7.71(1H, dd, J=8.4, 2.0Hz),
7.58(1H, d, J=2.0Hz), 6.88(1H, d, J=8.4Hz), 4.06(2H, t, J=6.6Hz),
4.04(2H, t, J=6.6Hz), 1.87-1.79(4H, m), 1.49-1.35(8H, m),
0.95-0.90(6H, m).

FABMS (+) (m/z) : 295[M + 1] (52),
294[M](80), 277(29), 224(32).

Preparative Example 50

3-Hydroxy-4-nitrobenzoic acid (5 g, 27.4 mmol), DMF (40 ml), potassium carbonate (13.8 g, 100 mmol) and pentyl bromide (8.7 ml, 70 mmol) were mixed, and this solution was stirred at 100°C for 1.5 hours. The reaction mixture was filtered to remove the inorganic salt, and DMF was evaporated under reduced pressure. Ethyl acetate (100 ml) was added to the obtained residue, and the mixture was washed 3 times with saturated brine (30 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Ethanol (150 ml) and 10% palladium-carbon catalyst (0.5 g) were added to the obtained residue, and the

mixture was stirred at room temperature for 5.5 hours in a stream of hydrogen. The palladium-carbon catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=5/1) to give pentyl 4-amino-3-pentyloxybenzoate (5.72 g, 70% in 2 steps) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.53(1H, dd, $J=8.2, 1.7\text{Hz}$), 7.44(1H, d, $J=1.7\text{Hz}$), 6.66(1H, d, $J=8.2\text{Hz}$), 4.26(2H, t, $J=6.7\text{Hz}$), 4.20(2H, bs), 4.05(2H, t, $J=6.5\text{Hz}$), 1.86-1.65(4H, m), 1.50-1.30(8H, m), 1.0-0.85(6H, m).

FABMS (m/z) : 294 [$\text{M} + \text{H}^+$] (80), 224(50), 206(50).

Preparative Example 51

Pentyl 4-amino-3-pentyloxybenzoate (1 g, 3.41 mmol), acetone (5 ml), potassium carbonate (0.83 g, 6 mmol) and methyl iodide (4 ml) were mixed, and this solution was refluxed under heating for 9 hours. The reaction mixture was filtered to remove the inorganic salt, and acetone was evaporated under reduced pressure. Ethanol (10 ml) and a 1N aqueous sodium hydroxide solution (10 ml) were added to the obtained residue, and the mixture was refluxed under heating for 2.5 hours. Ethanol was evaporated under reduced pressure, and conc. hydrochloric acid was added to make this solution acidic. The aqueous layer was extracted 3 times with ethyl acetate (20 ml). The organic layers were combined, washed 3 times with saturated brine (20 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=1/1) to give 4-dimethylamino-3-pentyloxybenzoic acid (146 mg, 17% in 2 steps) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.68(1H, dd, $J=8.1, 1.5\text{Hz}$), 7.53(1H, d, $J=1.8\text{Hz}$), 6.85(1H, d, $J=8.1\text{Hz}$), 4.06(2H, t, $J=6.8\text{Hz}$), 2.93(6H, s), 1.93-1.80(2H, m), 1.50-1.30(4H, m), 0.94(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z) : 252 [$\text{M} + \text{H}^+$] (100), 181(30).

Preparative Example 52

4-Methoxy-3-nitrobenzoic acid (5 g, 25.4 mmol), DMF (30 ml), potassium carbonate (5.53 g, 40 mmol) and pentyl bromide (4 ml, 32.3 mmol) were mixed,

and this solution was stirred at 100°C for 1.5 hours. The reaction mixture was filtered to remove the inorganic salt, and DMF was evaporated under reduced pressure. Ethyl acetate (100 ml) was added to the obtained residue. The mixture was washed 3 times with saturated brine (30 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Ethanol (150 ml) and 10% palladium-carbon catalyst (0.5 g) were added to the obtained residue, and the mixture was stirred at room temperature for 5.5 hours in a stream of hydrogen. The palladium-carbon catalyst was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=3/1) to give 3-amino-4-methoxybenzoic acid (5.98 g, 99% in 2 steps) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.48(1H, dd, $J=8.3, 1.9\text{Hz}$), 7.38(1H, d, $J=2.1\text{Hz}$), 6.79(1H, d, $J=8.3\text{Hz}$), 4.26(2H, t, $J=6.7\text{Hz}$), 4.09(3H, s), 3.86(2H, bs), 1.78-1.66(2H, m), 1.47-1.29(4H, m), 0.93(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 238 [$\text{M} + \text{H}^+$] (60), 237(100).

Preparative Example 53

3-Amino-4-methoxybenzoic acid (1.53 g, 6.45 mmol), DMF (15 ml), potassium carbonate (2.07 g, 15 mmol) and pentyl bromide (1.86 ml, 15 mmol) were mixed, and the solution was stirred at 100°C for 10.5 hours. The reaction mixture was filtered to remove the inorganic salt, and DMF was evaporated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=10/1) to give pentyl 4-methoxy-3-pentylaminobenzoate (1.32 g, 67%) and pentyl 3-dimethylamino-4-methoxybenzoate (334 mg, 14%) as colorless oils.

pentyl 4-methoxy-3-pentylaminobenzoate

$^1\text{H-NMR}$ (CDCl_3) δ : 7.41(1H, dd, $J=8.1, 2.1\text{Hz}$), 7.24(1H, d, $J=2.1\text{Hz}$), 6.75(1H, d, $J=8.1\text{Hz}$), 4.27(2H, t, $J=6.6\text{Hz}$), 4.20(1H, bs), 3.90(3H, s), 3.17(2H, t, $J=7.2\text{Hz}$), 1.82-1.62(4H, m), 1.5-1.3(8H, m), 0.93(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z) : 308 [$\text{M} + \text{H}^+$] (50), 307(100), 250(50).

pentyl 3-dimethylamino-4-methoxybenzoate

$^1\text{H-NMR}$ (CDCl_3) δ : 7.67(1H, dd, $J=8.5$, 2.1Hz),
7.66(1H, d, $J=2.0\text{Hz}$), 6.84(1H, d, $J=8.5\text{Hz}$), 4.28(2H, t, $J=6.7\text{Hz}$),
3.89(3H, s), 3.08(4H, t, $J=7.7\text{Hz}$), 1.80-1.70(2H, m), 1.5-1.18(16H, m),
0.93(3H, t, $J=7.1\text{Hz}$), 0.86(3H, t, $J=7.0\text{Hz}$).
FABMS (m/z) : 378 [$\text{M} + \text{H}^+$] (100), 320(100), 264(40).

Preparative Example 54

Ethanol (3 ml) and a 1N aqueous sodium hydroxide solution (3 ml) were added to pentyl 4-methoxy-3-pentylaminobenzoate (500 mg, 1.63 mmol), and the mixture was refluxed under heating for 2 hours. Ethanol was evaporated under reduced pressure. Conc. hydrochloric acid was added to neutralize this solution, and the aqueous layer was extracted 3 times with ethyl acetate (5 ml). The organic layers were combined, washed 3 times with saturated brine (5 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained crude crystals were purified by washing with hexane to give 4-methoxy-3-pentylaminobenzoic acid (356 mg, 71%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.51(1H, dd, $J=8.1$, 2.1Hz),
7.29(1H, d, $J=2.1\text{Hz}$), 6.78(1H, d, $J=8.1\text{Hz}$), 3.92(3H, s),
3.18(2H, t, $J=7.2\text{Hz}$), 1.75-1.6(2H, m), 1.5-1.3(4H, m),
0.93(3H, t, $J=6.5\text{Hz}$).
FABMS (m/z) : 238 [$\text{M} + \text{H}^+$] (80), 180(70).

Preparative Example 55

(4-Hydroxyphenyl)acetonitrile (12.6 g, 0.094 mol, 1 eq) was dissolved in DMF (60 ml), and to this solution were successively added benzyl bromide (12.4 ml, 0.104 mol, 1.1 eq) and anhydrous potassium carbonate (19.6 g, 0.14 mol, 1.5 eq). The mixture was stirred under heating at 90°C for 1.5 hours. This reaction mixture was cooled to room temperature. Water (200 ml) was added, and the mixture was extracted twice with ethyl ether (400 ml). The organic layers were combined, washed with saturated brine (800 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure and recrystallized from ethyl ether to give

4-benzyloxyphenylacetonitrile (11.1 g, 52.7%) as colorless needles.

m.p. : 67.9-68.2°C

$^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.3(5H, m), 7.23(2H, d, $J=8.7\text{Hz}$),

6.97(2H, d, $J=8.7\text{Hz}$), 5.06(2H, s), 3.67(2H, s).

FABMS (m/z) : 223 $[\text{M} + \text{H}^+]$ (40).

IR (KBr, cm^{-1}) : 3438, 2247, 1615, 1514, 1247, 1014.

Elemental analysis : $\text{C}_{15}\text{H}_{13}\text{NO}_4$

Calculated C 80.69, H 5.87, N 6.27

Found C 80.48, H 5.83, N 6.33

Preparative Example 56

LAH (2.82 g, 0.15 mol, 1.5 eq) was dissolved in THF (50 ml), and to this solution was added dropwise a THF solution (50 ml) of 4-benzyloxyphenylacetonitrile (11.1 g, 0.05 mol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was refluxed under heating for 1.5 hours. The reaction mixture was cooled to room temperature, and a saturated aqueous sodium sulfate solution (about 40 ml) was added under ice-cooling. After filtration through Celite, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (chloroform/methanol=10/1) to give 2-(4-benzyloxyphenyl)ethylamine (2.02 g, 17.9%) as colorless needles.

m.p. : 58.7-59.6°C

$^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.3(5H, m), 7.11(2H, d, $J=8.6\text{Hz}$),

6.92(2H, d, $J=8.6\text{Hz}$), 5.04(2H, s), 2.93(2H, t, $J=6.8\text{Hz}$),

2.69(2H, t, $J=6.8\text{Hz}$), 1.57(2H, bs).

FABMS (m/z) : 228 $[\text{M} + \text{H}^+]$ (40).

IR (KBr, cm^{-1}) : 3360, 2864, 1611, 1513, 1248.

Preparative Example 57

3-Hydroxyphenylacetonitrile (834 mg, 6.26 mmol) was dissolved in DMF (10 ml), and to this solution were successively added benzyl bromide (0.82 ml, 6.89 mmol, 1.1 eq) and anhydrous potassium carbonate (1.30 g, 9.40 mmol, 1.5 eq). The mixture was stirred under heating at 90°C for 1.5 hours. This reaction mixture was cooled to room temperature, and water (20 ml) was added. The

mixture was extracted twice with ethyl acetate (40 ml). The organic layers were combined, washed with saturated brine (80 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate=1/1) to give (3-benzyloxyphenyl)acetonitrile (1.21 g, 86.8%).
 $^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.3(6H, m), 7.0-6.9(3H, m), 5.09(2H, s), 3.72(2H, s).

Preparative Example 58

LAH (0.615 g, 0.0162 mol, 3.0 eq) was dissolved in THF (20 ml), and to this solution was added dropwise a THF solution (20 ml) of (3-benzyloxyphenyl)-acetonitrile (1.2 g, 0.0054 mol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was refluxed under heating for 3 hours. The reaction mixture was cooled to room temperature, and a saturated aqueous sodium sulfate solution (about 30-40 ml) was added under ice-cooling. After filtration through Celite, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (chloroform/methanol=10/1) to give 2-(3-benzyloxyphenyl)ethylamine (0.434 g, 35.3%) as a pale-yellow amorphous.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.2(6H, m), 6.8-6.7(3H, m), 5.09(2H, s), 2.95(2H, t, $J=7.0\text{Hz}$), 2.70(2H, t, $J=7.0\text{Hz}$), 2.01(2H, bs).
 FABMS (m/z) : 228 [$\text{M} + \text{H}^+$] (90).

Preparative Example 59

10% Palladium-carbon catalyst (water content 50%, 86 mg) was added to a solution of 2-(3-benzyloxyphenyl)ethylamine (434 mg, 1.91 mmol, 1.0 eq) in THF (10 ml), and the mixture was stirred at room temperature for 3 hours in a stream of hydrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to give 2-(3-hydroxyphenyl)ethylamine (250 mg, 95.5%).

$^1\text{H-NMR}$ (CDCl_3) δ : 8.26(1H, bs), 7.1-6.9(1H, m), 6.7-6.6(1H, m), 6.6-6.4(2H, m), 2.7-2.6(2H, m), 2.6-2.5(2H, m), 3.5(2H, bs).
 FABMS (m/z) : 138 [$\text{M} + \text{H}^+$] (30).

Preparative Example 60

(2-Hydroxyphenyl)acetonitrile (1.01 g, 0.0076 mol) was dissolved in DMF (10 ml), and to this solution were successively added benzyl bromide (0.90 ml, 0.0076 mol, 1.0 eq) and anhydrous potassium carbonate (2.1 g, 0.015 mol, 3.0 eq). The mixture was stirred with heating at 90°C for 1.5 hours. The reaction mixture was cooled to room temperature, and water (10 ml) was added. The mixture was extracted twice with ethyl acetate (30 ml). The organic layers were combined, washed with saturated brine (60 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give (2-benzyloxyphenyl)acetonitrile (2.04 g, 100%) as a colorless solid.

Preparative Example 61

LAH (1.04 g, 0.0273 mol, 3.0 eq) was dissolved in THF (25 ml), and to this solution was added dropwise a THF solution (25 ml) of (2-benzyloxyphenyl)-acetonitrile (2.04 g, 0.0091 mol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was stirred at room temperature for 15 minutes and refluxed under heating for 2 hours. This reaction mixture was cooled with ice-cold water, and a saturated aqueous sodium sulfate solution (about 30-40 ml) was added. After filtration through Celite, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (chloroform/methanol=5/1) to give 2-(2-benzyloxyphenyl)ethylamine (0.415 g, 20.0%) as a pale-yellow amorphous compound.
FABMS (m/z) : 228[M + H⁺] (100).

Preparative Example 62

10% Palladium-carbon catalyst (water content 50%, 42 mg) was added to a solution of 2-(2-benzyloxyphenyl)ethylamine (415 mg, 1.826 mmol, 1.0 eq) in THF (10 ml), and the mixture was stirred for 2 hours at room temperature in a stream of hydrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to give 2-(2-hydroxyphenyl)ethylamine (230 mg, 91.8%).

Preparative Example 63

3-(4-Hydroxyphenyl)propionitrile (1.47 g, 0.01 mol) was dissolved in DMF (24 ml), and to this solution were successively added benzyl bromide (1.31 ml, 0.011

mol, 1.1 eq) and anhydrous potassium carbonate (4.15 g, 0.030 mol, 3.0 eq). The mixture was stirred under heating at 90°C for 3 hours. This reaction mixture was cooled to room temperature, and water (100 ml) was added. The mixture was extracted twice with ethyl acetate (100 ml). The organic layers were combined, washed with saturated brine (200 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 3-(4-benzyloxyphenyl)propionitrile (2.39 g, 100%) as a colorless solid.

Preparative Example 64

LAH (570 mg, 0.015 mol, 1.5 eq) was dissolved in THF (30 ml), and to this solution was added dropwise a THF solution (50 ml) of 3-(4-benzyloxyphenyl)propionitrile (2.37 g, 0.01 mol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was stirred at room temperature for 2 hours. This reaction mixture was cooled with ice-cold water, and a saturated aqueous sodium sulfate solution (about 30-40 ml) was added. After filtration through Celite, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (chloroform/methanol=10/1-5/1) to give 3-(4-benzyloxyphenyl)propylamine (1.2 g, 49.7%) as a pale-yellow amorphous compound.

¹H-NMR (CDCl₃) δ : 7.4-7.3(5H, m), 7.10(2H, d, J=8.6Hz), 6.90(2H, d, J=8.6Hz), 5.04(2H, s), 3.48(2H, s), 2.72(2H, d, J=7.1Hz), 2.60(2H, t, J=7.7Hz), 1.8-1.7(2H, m).

FABMS (m/z) : 242[M + H⁺] (100).

Preparative Example 65

10% Palladium-carbon catalyst (water content 50%, 120 mg) was added to a solution of 3-(4-benzyloxyphenyl)propylamine (620 mg, 2.57 mmol, 1.0 eq) in THF (10 ml), and the mixture was stirred for 2 hours at room temperature in a stream of hydrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to give 3-(4-hydroxyphenyl)propylamine (354 mg, 91.1%).

¹H-NMR (CDCl₃) δ : 7.0(2H, d, J=9Hz), 6.7(2H, d, J=9Hz), 3.0(3H, bs), 2.7(2H, t, J=7.5Hz), 2.6(2H, t, J=7.5Hz), 1.8-1.7(2H, m).

FABMS (m/z) : 152[M + H⁺] (100).

Preparative Example 66

LAH (570 mg, 0.015 mol, 1.5 eq) was dissolved in THF (30 ml), and to this solution was added dropwise a THF solution (30 ml) of 4-benzyloxybenzonitrile (2.09 g, 0.01 mol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was heated to room temperature and refluxed under heating for 3 hours. This reaction mixture was cooled with ice-cold water, and a saturated aqueous sodium sulfate solution (about 30-40 ml) was added. After filtration through Celite, the filtrate was concentrated under reduced pressure to give 4-benzyloxybenzylamine (2.03 g, 95.1%) as a pale-yellow amorphous compound.

¹H-NMR (CDCl₃) δ : 7.4-7.3(5H, m), 7.22(2H, d, J=8.6Hz), 6.94(2H, d, J=8.6Hz), 5.05(2H, s), 3.80(2H, s), 1.50(2H, s).

FABMS (m/z) : 214[M + H⁺] (60), 197(100).

Preparative Example 67

10% Palladium-carbon catalyst (water content 50%, 50 mg) was added to a solution of 4-benzyloxybenzylamine (530 mg, 2.485 mmol, 1.0 eq) in THF (10 ml), and the mixture was stirred for 3 hours at room temperature in a stream of hydrogen. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=1/1) to give 4-hydroxybenzylamine (260 mg, 85.0%).

¹H-NMR (CDCl₃) δ : 7.1(2H, d, J=9Hz), 6.77(2H, d, J=9Hz), 3.8(2H, s), 2.9(3H, bs).

FABMS (m/z) : 124[M + H⁺] (80).

Preparative Example 68

2-(4-Hydroxyphenyl)ethylamine (1.37 g, 10.0 mmol, 1.0 eq) was dissolved in acetic acid (10 ml), and platinum dioxide catalyst (137 mg) was added. The mixture was stirred at 3 kgf/cm² in a stream of hydrogen at 70°C for 5 hours. The reaction mixture was filtered through Celite and the catalyst was washed with toluene. The filtrate was concentrated under reduced pressure to give 2-(4-hydroxycyclohexyl)ethylamine (1.8 g).

$^1\text{H-NMR}$ (CDCl_3) δ : 8.76(1H, bs), 3.9(0.5H, bs),
3.6-3.5(0.5H, m), 3.0-2.8(4H, m), 2.2-0.8(9H, m).
FABMS (m/z) : 144 $[\text{M} + \text{H}^+]$ (20), 128(100).

Preparative Example 69

LAH (1.90 g, 50 mmol) was suspended in diethyl ether (150 ml), and a solution of 3-pyridylacetonitrile (5.91 g, 50 mmol, 1.0 eq) in diethyl ether (150 ml) was added at room temperature. The mixture was stirred at room temperature for 14 hours. To this reaction mixture were successively added water (1.9 ml), a 15% aqueous sodium hydroxide solution (1.9 ml) and water (5.7 ml). The resulting precipitate was filtered through Celite and washed with diethyl ether, which was followed by concentration under reduced pressure. The obtained residue was subjected to column chromatography (chloroform/methanol=30/1 - chloroform/methanol/triethylamine=8/2/0.1) to give 2-(3-pyridyl)ethylamine (2.39 g, 39%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :
8.48-8.46(2H, m), 7.55-7.52(1H, m), 7.25-7.16(1H, m),
2.99(2H, t, $J=7.5\text{Hz}$), 2.76(2H, t, $J=7.5\text{Hz}$).
FABMS (+) (m/z) : 123 $[\text{M} + 1]$ (100).

Preparative Example 70

4-Vinylpyridine (5.26 ml, 50 mmol) and ammonium chloride (5.35 g, 100 mmol, 2.0 eq) were dissolved in methanol (2.5 ml) and water (15 ml), and the mixture was stirred with reflux for 23 hours. This reaction mixture was poured into ice water, and a 15% aqueous sodium hydroxide solution was added to make the same strong alkaline. The mixture was extracted 3 times with chloroform (50 ml). The organic layers were combined, washed with saturated brine and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was distilled under reduced pressure to give 2-(4-pyridyl)ethylamine (①) (1.80 g, 30%; 87°C/6 mmHg) as a colorless oil. The residue from the distillation was subjected to column chromatography (chloroform/methanol=30/1-9/1) to give bis[2-(4-pyridyl)ethyl]amine (②) (1.11 g, 20%) as a pale-yellow oil.

① : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.53-8.51(2H, m), 7.15-7.13(2H, m), 3.04-2.98(2H, m),
2.75(2H, t, J=8.4Hz).

FABMS (+) (m/z) : 123[M + 1] (100).

② : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.47-8.42(4H, m), 7.11-7.09(4H, m), 2.95-2.90(4H, m),
2.77(4H, t, J=7.1Hz).

FABMS (+) (m/z) : 228[M + 1] (100).

Preparative Example 71

2-Vinylpyridine (5.26 g, 50 mmol) and ammonium chloride (13.4 g, 250 mmol, 5.0 eq) were dissolved in methanol (2.5 ml) and water (15 ml), and the mixture was stirred with reflux for 7 hours. This reaction mixture was poured into ice water, and a 15% aqueous sodium hydroxide solution was added to make the same strong alkaline. The mixture was extracted 3 times with chloroform (50 ml). The organic layers were combined, washed with saturated brine and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was distilled under reduced pressure to give 2-(2-pyridine)ethylamine.

① (2.55 g, 42%; 77-78°C/6 mmHg) as a colorless oil. The residue from the distillation was subjected to column chromatography (chloroform/methanol=10/1) to give bis[2-(2-pyridyl)ethyl]amine ② (2.04 g, 36%) as a pale-yellow oil.

① : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.56-8.52(4H, m), 7.60(1H, td, J=7.60, 1.80Hz), 7.17(1H, d, J=7.6Hz),
7.16-7.09(1H, m), 3.12(2H, t, J=6.7Hz), 2.93(2H, t, J=6.7Hz).

FABMS (+) (m/z) : 123[M + 1] (100), 106(45).

② : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.48(2H, d, J=4.8Hz), 7.57(2H, td, J=7.6, 1.7Hz), 7.14(2H, d, J=7.6Hz),
7.12-7.08(2H, m), 3.10-2.96(8H, m), 2.41(1H, brs).

FABMS (+) (m/z) : 228[M + 1] (100), 135(80).

Preparative Example 72

2-(4-Hydroxyphenyl)ethylamine (5.0 g, 0.0364 mol, 1 eq) was dissolved in formic acid (77 ml, 2.04 mol, 56 eq), and acetic anhydride (25.4 ml, 0.27 mol, 7.4 eq) was added to this solution at 5-15°C. The mixture was stirred at room

temperature for 3 hours. Ice-cold water (30 ml) was added to this reaction mixture, and the mixture was concentrated under reduced pressure. Water (50 ml) was added to the residue, and the mixture was extracted twice with ethyl acetate (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 2-(4-hydroxyphenyl)ethyl-N-formamide (6.6 g, 100%) as an oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 8.69(1H, s), 8.09(1H, s), 7.41(2H, d, $J=8.7\text{Hz}$), 6.60(2H, d, $J=8.7\text{Hz}$), 3.83(2H, t, $J=4.9\text{Hz}$), 3.51(2H, t, $J=4.9\text{Hz}$).

FABMS (m/z) : 166(100).

Preparative Example 73

LAH (2.14 g, 0.056 mol, 3 eq) was dissolved in THF (30 ml), and to this solution was added dropwise a THF solution (30 ml) of 2-(4-hydroxyphenyl)ethyl-N-formamide (3.1 g, 0.0188 mol, 1 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was heated to room temperature and refluxed under heating for 5 hours. This reaction mixture was cooled with ice-cold water, and a saturated aqueous sodium sulfate solution (about 10-20 ml) was added. After filtration of this reaction mixture through Celite, the filtrate was concentrated under reduced pressure to give 2-(4-hydroxyphenyl)ethyl-N-methylamine (2.81 g, 99.0%).

$^1\text{H-NMR}$ (CDCl_3) δ : 7.1-6.9(2H, m), 6.7-6.6(2H, m), 4.0(1H, bs), 2.9-2.7(2H, m), 2.7-2.6(2H, m), 2.31(3H, m).

FABMS (m/z) : 152(60), 121(80).

Preparative Example 74

(1) Benzene (20 ml) and N,N' -dimethylethylenediamine (1.56 ml, 14.7 mmol) were added to 4-methoxybenzaldehyde (2 g, 14.7 mmol), and the mixture was refluxed under heating for 5 hours while removing the generated water. Benzene was evaporated to give a crude product of 2-(4-methoxyphenyl)-1,3-dimethylimidazolidine.

(2) The above crude product (0.5 g, 2.42 mmol), THF (6 ml) and tetramethylethylenediamine (0.73 ml, 4.84 mmol) were mixed, and this solution was cooled to

-78°C. n-Butyllithium (3 ml of 1.6M hexane solution, 4.84 mmol) was added and the mixture was stirred at 0°C for 2 hours. This solution was cooled to -78°C, and di-n-amyldisulfide (1.07 ml, 4.84 mmol) was added. The mixture was stirred at room temperature for 11.5 hours. Water (5 ml) was added and the aqueous layer was extracted 3 times with ethyl acetate (5 ml). The organic layers were combined and washed with saturated brine (5 ml). The filtrate was concentrated under reduced pressure. A 10% aqueous sulfuric acid solution was added to the obtained residue and the mixture was stirred for 2 days. The aqueous layer was extracted 4 times with ethyl acetate (10 ml). The organic layers were combined and washed twice with saturated brine (5 ml). The filtrate was concentrated under reduced. The obtained residue was purified by column chromatography (hexane/ethyl acetate = 20/1 - 10/1) to give 4-methoxy-3-pentylthiobenzaldehyde (437 mg, 76%) as a pale-yellow oil.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 9.87(1H, s), 7.74(1H, d, $J=2.1\text{Hz}$), 7.66(1H, dd, $J=8.1, 1.8\text{Hz}$), 6.95(1H, d, $J=8.1\text{Hz}$), 3.98(3H, s), 2.95(2H, t, $J=7.4\text{Hz}$), 1.62-1.80(2H, m), 1.20-1.55(4H, m), 0.91(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z) : 289 [$\text{M} + \text{H}^+$] (100), 237 (70).

Preparative Example 76

A suspension of isovanillin (200 g, 1.341 mmol), acetic acid (700 ml) and concentrated sulfuric acid (0.2 ml) was cooled to 0°C, a solution (200 ml) of fuming nitric acid (57.2 ml, 1.38 mol) in acetic acid was added dropwise over 30 minutes. After stirring for 40 minutes, water (400 ml) was added, and the generated crystals were collected by filtration to give a mixture of 3-hydroxy-4-methoxy-2-nitrobenzaldehyde and 3-hydroxy-4-methoxy-6-nitrobenzaldehyde (156.4 g, 60.4%).

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 10.1(1H, s), 7.46(1H, d, $J=8.4\text{Hz}$), 7.12(1H, d, $J=8.4\text{Hz}$), 4.03(3H, s).

Preparative Example 77

A mixture of 3-hydroxy-4-methoxy-2-nitrobenzaldehyde and 3-hydroxy-4-methoxy-6-nitrobenzaldehyde, and DMF (700 ml) were mixed, and potassium carbonate (136.7 mg, 989 mmol) and bromopentane (122.7 ml, 989 mmol) were

successively added to this solution. The reaction mixture was stirred at 100°C for 4 hours and filtered. Water (600 ml) and hexane-ethyl acetate (1:1, 600 ml) were added to the filtrate for separation. The aqueous layer was extracted with hexane-ethyl acetate (1:1, 600 ml). The organic layers were combined, and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was evaporated. The precipitated crystals were collected by filtration to give 4-methoxy-6-nitro-3-pentyloxybenzaldehyde (②) (90.1 g, 44%) as yellow crystals. The filtrate after filtration of said crystals was further evaporated to give 4-methoxy-2-nitro-3-pentyloxybenzaldehyde (①) (117 g, 58%) as a red oil.

①: $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 9.80(1H, s), 7.64(1H, d, $J=8.6\text{Hz}$), 7.09(1H, d, $J=8.6\text{Hz}$), 4.11(2H, t, $J=6.6\text{Hz}$), 3.99(3H, s), 1.60-1.80(2H, m), 1.28-1.47(4H, m), 0.92(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 268 [$\text{M} + \text{H}^+$] (80), 198 (100).

②: $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 10.4(1H, s), 7.61(1H, s), 7.39(1H, s), 4.16(2H, t, $J=6.8\text{Hz}$), 1.82-1.95(2H, m), 1.30-1.50(4H, m), 0.94(3H, t, $J=7.2\text{Hz}$).

Preparative Example 78

4-Methoxy-2-nitro-3-pentyloxybenzaldehyde (70 g, 261.9 mmol), amidosulfuric acid (76.3 g, 785.7 mmol) and isopropanol (210 ml) were mixed, an aqueous sodium chlorite (38.5 g, 340.5 mmol) solution (350 ml) was added dropwise to this solution while cooling in a water bath. After stirring for 20 minutes, ethyl acetate (300 ml) was added to separate the organic layer. The aqueous layer was extracted with ethyl acetate (200 ml). The organic layers were combined, washed with saturated brine (150 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The precipitated crystals were collected by filtration to give 4-methoxy-2-nitro-3-pentyloxybenzoic acid (59.02 g, 80%) as pale-yellow crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 7.85(1H, d, $J=8.8\text{Hz}$), 7.02(1H, d, $J=8.8\text{Hz}$), 4.08(2H, t, $J=6.7\text{Hz}$), 3.98(3H, s), 1.95-1.80(2H, m), 1.30-1.45(4H, m), 0.93(3H, t, $J=7.0\text{Hz}$).

FABMS (m/z) : 284 [$\text{M} + \text{H}^+$] (30), 266 (30), 196 (100).

Preparative Example 79

4-Methoxy-2-nitro-3-pentyloxybenzoic acid (26.8 g, 94.6 mmol) and ethanol (350 ml) were mixed, and 10% palladium-carbon catalyst (2.6 g) was added to this solution. The reaction mixture was stirred at room temperature for 7.5 hours in a hydrogen gas stream (3 kgf/cm²) and filtered. The filtrate was concentrated under reduced pressure, and the precipitated crystals were collected by filtration to give 2-amino-4-methoxy-3-pentyloxybenzoic acid (22.7 g, 95%) as gray crystals. ¹H-NMR (CDCl₃, 300MHz) δ : 7.87(1H, d, J=9.0Hz), 6.31(1H, d, J=9.0Hz), 3.94(2H, t, J=6.8Hz), 3.89(3H, s), 1.70-1.88(2H, m), 1.30-1.54(4H, m), 0.94(3H, t, J=7.1Hz).

Preparative Example 80

Pentyl 3-amino-4-methoxybenzoate (0.744 g, 4.45 mmol), methylene chloride (15 ml) and dimethylsulfide (0.33 ml, 4.50 mmol) were mixed, and after cooling to -30°C, N-chlorosuccinimide (601 mg, 4.5 mmol) was added to this solution. After stirring for 1 hour, triethylamine (0.627 ml, 4.5 mmol) was added, and the mixture was refluxed under heating for 0.5 hour. Saturated brine (0.5 ml) was added to stop the reaction, the reaction mixture was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate = 4/1) to give pentyl 3-amino-4-methoxy-2-methylthiomethylbenzoate (0.83 g, 82%) as a brown oil.

¹H-NMR (CDCl₃, 300MHz) δ : 7.40(1H, d, J=8.6Hz), 6.74(1H, d, J=8.6Hz), 4.40(2H, bs), 4.26(2H, t, J=6.7Hz), 4.22(2H, s), 3.90(3H, s), 2.05(3H, s), 1.65-1.80(2H, m), 1.30-1.50(4H, m), 0.93(3H, t, J=7.1Hz).
FABMS (m/z) : 298[M + H⁺](10), 297(50), 250(50).

Preparative Example 81

Pentyl 3-amino-4-methoxy-2-methylthiomethylbenzoate (830 mg, 2.79 mmol) and DMF (4.0 ml) were mixed, and potassium t-butoxide (470 mg, 4.19 mmol) and bromopentane (0.62 ml, 5.0 mmol) were successively added to this solution. The mixture was stirred at 100°C for 1 hour and filtered. The filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (hexane/ethyl acetate = 15/1) to give pentyl 4-methoxy-2-methylthiomethyl-3-pentylaminobenzoate (178 mg, 17%) as a pale-yellow oil.

¹H-NMR (CDCl₃, 300MHz) δ : 7.54(1H, d, J=8.7Hz), 6.75(1H, d, J=8.7Hz),

4.27(2H, t, J=6.7Hz), 4.23(2H, s), 3.88(3H, s), 3.73(1H, bs),
3.05(2H, t, J=7.1Hz), 2.02(3H, s), 1.70-1.85(2H, m), 1.30-1.50(10H, m),
0.83-0.97(6H, m).

Preparative Example 82

Pentyl 4-methoxy-2-methylthiomethyl-3-pentylaminobenzoate (173 mg, 0.47 mmol) was hydrolyzed in the same manner as in Preparative Example 45 to give 4-methoxy-2-methylthiomethyl-3-pentylaminobenzoic acid (93 mg, 66%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 7.74(1H, d, J=8.6Hz), 6.80(1H, d, J=8.6Hz),
4.31(2H, s), 3.92(3H, s), 3.09(2H, t, J=7.1Hz), 2.08(3H, s),
1.50-1.65(2H, m), 1.30-1.45(4H, m), 0.94(3H, t, 7.0Hz).
FABMS (m/z) : 298[M + H⁺](50), 250(50), 185(85).

Preparative Example 83

2-(4-Methoxy-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (500 mg, 1.76 mmol) and DMF (8 ml) were mixed, and this solution was cooled to -60°C. n-Butyllithium (1.6 M hexane solution, 2.42 ml, 3.87 mmol) was added and the mixture was stirred for 1 hour. Dimethyl disulfide (0.35 ml, 3.87 mmol) was added to this solution, and the mixture was stirred at room temperature for 1 hour. Water (5 ml) was added, and the aqueous layer was extracted 3 times with ethyl acetate (10 ml). The organic layers were combined and concentrated under reduced pressure. A 3N hydrochloric acid (4 ml) was added to the obtained residue and the mixture was under heating for 3 hours. A 10N aqueous sodium hydroxide solution (4 ml) was added and the mixture was refluxed under heating for 2 hours. A concentrated hydrochloric acid (3 ml) was added to make the reaction mixture acidic, and the aqueous layer was extracted 4 times with ethyl acetate (20 ml). The organic layers were combined, washed 3 times with saturated brine (10 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained crude crystals were purified by washing with hexane to give 4-methoxy-2-methylthio-3-pentyloxybenzoic acid (370 mg, 74%) as pale-brown crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 8.10(1H, d, J=8.9Hz), 6.99(1H, d, J=8.9Hz),

4.02(2H, t, $J=6.6\text{Hz}$), 3.93(3H, s), 2.50(3H, s), 1.75-1.90(2H, m),
1.30-1.58(4H, m), 0.95(3H, t, 7.1Hz).

FABMS (m/z) : 285 $[M + H]^+$ (40), 267(100).

Preparative Example 84

4-Amino-3-pentyloxybenzoic acid (200 mg, 0.90 mmol), methylene chloride (5 ml) and pyridine (0.081 ml, 1.0 mmol) were mixed, and valeryl chloride (0.11 ml, 0.90 mmol) was added to this solution. The mixture was stirred at room temperature for 0.5 hour. Water was added to the reaction mixture, and the aqueous layer was extracted 3 times with ethyl acetate (5 ml). The organic layers were combined, washed with saturated brine (10 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained crude crystals were washed with hexane to give 4-pentanoylamino-3-pentyloxybenzoic acid (109.5 mg, 40%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 8.50(1H, d, $J=8.4\text{Hz}$), 7.98(1H, s),
7.73(1H, d, $J=8.4\text{Hz}$), 7.55(1H, s), 4.11(2H, t, $J=6.6\text{Hz}$),
2.43(2H, t, $J=7.5\text{Hz}$), 1.80-1.95(2H, m), 1.35-1.55(6H, m),
0.96(6H, t, 7.2Hz).

FABMS (m/z) : 308 $[M + H]^+$ (40), 206(100).

Preparative Example 85

(1) 2-Hydroxy-3-methoxybenzaldehyde (3.00 g, 19.7 mmol) and DMF (25 ml) were mixed, and potassium carbonate (3.00 g, 22.0 mmol) and bromopentane (2.73 ml, 22.0 mmol) were successively added to this solution. The reaction mixture was stirred at 100°C for 2 hours and the obtained solid was filtered. Water (20 ml) and ethyl acetate (50 ml) were added for separation. The aqueous layer was extracted twice with ethyl acetate (25 ml). The organic layers were combined, washed twice with saturated brine (20 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of 3-methoxy-2-pentyloxybenzaldehyde. (2) THF (30 ml) and methyl (triphenylphosphoranilidene)acetate (7.36 g, 22.0 mmol) were added to the above-mentioned compound. The mixture was refluxed under heating for 5.5 hours and THF was evaporated under reduced pressure.

Hexane (100 ml) was added to the obtained residue, and the precipitated crystals were filtered off. The filtrate was concentrated under reduced pressure. To the obtained residue were added ethanol (40 ml) and a 1N aqueous sodium hydroxide solution (40 ml). The mixture was refluxed under heating for 1 hour. After removing ethanol by evaporation under reduced pressure, concentrated hydrochloric acid was added to make the aqueous layer acidic. The aqueous layer was extracted twice with ethyl acetate (70 ml). The organic layers were combined, washed 3 times with saturated brine (40 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained crude crystals were recrystallized from ethyl acetate to give 3-(3-methoxy-2-pentyloxyphenyl)cinnamic acid (3.82 g, 73% in 3 steps) as colorless needles.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 8.17(1H, d, $J=16.2\text{Hz}$), 7.18(1H, d, $J=7.8\text{Hz}$), 7.06(1H, t, $J=7.8\text{Hz}$), 6.95(1H, d, $J=7.8\text{Hz}$), 6.48(1H, d, $J=16.2\text{Hz}$), 3.99(2H, t, $J=6.7\text{Hz}$), 3.86(3H, s), 1.75-1.85(2H, m), 1.37-1.49(4H, m), 0.94(3H, t, 7.2Hz).

FABMS (m/z) : 265 $[\text{M} + \text{H}^+]$ (20), 177(100).

Preparative Example 86

3-(3-Methoxy-2-pentyloxyphenyl)cinnamic acid (3.80 g, 14.4 mmol) was dissolved in ethanol (100 ml), and 10% palladium-carbon catalyst (0.38 g) was added to this solution. The reaction mixture was stirred for 1 hour in a stream of hydrogen and filtered. The filtrate was concentrated under reduced pressure to give 3-(3-methoxy-2-pentyloxyphenyl)propionic acid (3.42 g, 89%) as gray crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 6.96(1H, t, $J=7.9\text{Hz}$), 6.98(2H, d, $J=7.9\text{Hz}$), 3.95(2H, t, $J=6.7\text{Hz}$), 3.83(3H, s), 2.95(2H, t, $J=7.9\text{Hz}$), 2.66(2H, t, $J=7.9\text{Hz}$), 1.70-1.85(2H, m), 1.35-1.50(4H, m), 0.92(3H, t, 7.0Hz).

FABMS (m/z) : 267 $[\text{M} + \text{H}^+]$ (20), 179(100).

Preparative Example 87

3-(3-Methoxy-2-pentyloxyphenyl)propionic acid (1.00 g, 3.75 mmol), thionyl chloride (0.72 ml, 10 mmol) and one drop of DMF were mixed, and the mixture was stirred at room temperature for 15 minutes. Toluene (10 ml) was added and the

mixture was filtered. The filtrate was concentrated under reduced pressure. Acetone (5 ml) and a solution of sodium azide (0.33 g, 5.0 mmol) in water (0.5 ml) were added to the obtained residue, and the mixture was stirred at room temperature for 20 minutes. Water (5 ml) was added, and the aqueous layer was extracted twice with toluene (20 ml). The organic layers were combined, washed twice with saturated brine (10 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Toluene (10 ml) was added to the obtained residue. The mixture was refluxed under heating for 2.5 hours, and toluene was evaporated under reduced pressure. Polyphosphoric acid (3 ml) was added to the obtained residue and the mixture was stirred for 40 minutes. Water (20 ml) and ethyl acetate (50 ml) were added to separate the organic layer. The organic layer was washed successively with water (10 ml) and saturated brine (10 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Hexane (10 ml) was added to the obtained residue, and the precipitated crystals were collected by filtration to give 6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (829 mg, 84%) as colorless needles.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 7.84(1H, d, $J=8.4\text{Hz}$), 6.88(1H, d, $J=8.4\text{Hz}$), 6.04(1H, bs), 3.93(2H, t, $J=6.9\text{Hz}$), 3.90(3H, s), 3.49-3.55(2H, m), 3.02(2H, t, $J=6.6\text{Hz}$), 1.70-1.81(2H, m), 1.30-1.50(4H, m), 0.94(3H, t, 7.2Hz).

FABMS (m/z) : 264 [$\text{M} + \text{H}^+$] (100).

Preparative Example 88

3-Hydroxy-4-methoxybenzaldehyde (200 g, 1.31 mol), dioxane (1000 ml) and water (400 ml) were mixed, and N-bromosuccinimide (245.7 g, 1.38 mol) was added over 10 minutes. After 60 and 70 minutes, N-bromosuccinimide was further added in an amount of 16.4 g (92.1 mmol) and 7.02 g (39.4 mmol), respectively, and the mixture was further stirred for 30 minutes. Water (1600 ml) was added, and the precipitated crystals were collected by filtration. The crystals were washed with water (1000 ml) to give 2-bromo-3-hydroxy-4-methoxybenzaldehyde (227.1 g, 74.8%) as pale-red crystals.

$^1\text{H-NMR}$ ($\text{DMSO-}d_6$, 300MHz) δ : 10.1(1H, s), 9.59(1H, s), 7.40(1H, d, $J=8.4\text{Hz}$), 7.14(1H, d, $J=8.4\text{Hz}$), 3.92(3H, s).
 FABMS (m/z) : 232 $[\text{M} + \text{H}^+]$ (20), 185(100).

Preparative Example 89

(1) 2-Bromo-3-hydroxy-4-methoxybenzaldehyde (225.2 g, 975 mmol) and DMF (660 ml) were mixed, and potassium carbonate (148.2 g, 1.07 mol) and bromopentane (133 ml, 1.07 mol) were successively added to this solution. The mixture was stirred at 90°C for 1.5 hours and cooled to room temperature. Water (800 ml) was added to stop the reaction. The aqueous layer was extracted successively with diethyl ether (1000 ml, 500 ml) and ethyl acetate (500 ml). The organic layers were combined, washed successively with water (200 ml) and saturated brine (200 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of 2-bromo-4-methoxy-3-pentyloxybenzaldehyde.

(2) The above crude product, isopropanol (440 ml) and sulfamic acid (283.9 g, 2.92 mol) were mixed, and an aqueous sodium chlorite (purity 80%, 143.3 g, 1.27 mol) solution (1320 ml) was added dropwise to this solution under ice-cooling. The mixture was stirred at 40°C for 30 minutes, and water (1000 ml) was added. The precipitated crystals were collected by filtration and washed with water (2000 ml) to give 2-bromo-4-methoxy-3-pentyloxybenzoic acid (238.98 g, 77%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ : 7.83(1H, d, $J=8.7\text{Hz}$), 6.90(1H, d, $J=8.7\text{Hz}$), 3.98(2H, t, $J=6.7\text{Hz}$), 3.92(3H, s), 1.82-1.90(2H, m), 1.30-1.53(4H, m), 0.94(3H, t, $J=7.2\text{Hz}$).

FABMS (m/z) : 318 $[\text{M} + \text{H}^+]$ (10), 185(100).

Preparative Example 90

(1) 2-bromo-4-methoxy-3-pentyloxybenzoic acid (80.1 g, 253 mmol), toluene (480 ml), copper(I) bromide (3.62 g, 25.3 mmol) and diethyl malonate (153.4 ml, 1.01 mol) were mixed, and sodium hydride (60% dispersion, 30.3 g, 758 mmol) was added to this suspension. The mixture was stirred at 78°C - 83°C for 1 hour. Said reaction mixture was combined with a reaction mixture in which 2-bromo-4-methoxy-3-pentyloxybenzoic acid (49.43 g, 156 mmol) had been reacted in the

same manner, and the resulting reaction mixture was extracted with water (1000 ml, 500 ml). The aqueous layer was washed with hexane (500 ml).

Concentrated hydrochloric acid was added to make the aqueous layer acidic. The aqueous layer was extracted with ethyl acetate (1000 ml, 500 ml). The organic layers were combined, and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of diethyl 2-(6-carboxy-3-methoxy-2-pentyloxyphenyl)-malonate.

(2) The above crude product, lithium chloride (51.93 g, 1.23 mol), water (7.35 ml, 408 mmol) and DMSO (405 ml) were mixed, and the mixture was stirred at 140°C for 1 hour. Water (600 ml) and ethyl acetate (800 ml) were added to the reaction mixture, and the organic layer was separated and extracted twice with water (300 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. Hexane (250 ml) was added to the obtained residue. The precipitated crystals were collected by filtration and washed with hexane (150 ml) to give 2-ethoxycarbonylmethyl-4-methoxy-3-pentyloxybenzoic acid (99.93 g, 75.3% in 2 steps) as pale-brown crystals.

¹H-NMR (CDCl₃, 300MHz) δ : 7.93(1H, d, J=8.7Hz), 6.88(1H, d, J=8.7Hz), 4.12-4.22(4H, m), 3.93(2H, t, J=6.6Hz), 3.93(3H, s), 1.70-1.88(2H, m), 1.35-1.55(4H, m), 1.26(3H, t, 7.2Hz), 0.93(3H, t, 6.9Hz).

FABMS (m/z) : 323[M + H⁺](70), 227(90).

Preparative Examples 91-131

The compounds shown in Preparative Examples 91-131 were obtained in the same manner as in the above-mentioned Preparative Examples 1-90. The properties of said compounds are shown in Tables 1-14.

Example 1-1

4-Methoxy-3-pentyloxybenzoic acid (5.29 g, 0.02 mol, 1.0 eq) and 1-hydroxybenzotriazole hydrate (2.7 g, 0.024 mol, 1.0 eq) were dissolved in DMF (50 ml), and to this solution were successively added 2-(4-hydroxyphenyl)ethylamine (4.1 g, 0.03 mol, 1.5 eq) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) hydrochloride (4.6 g, 0.024 mol, 1.2 eq) under ice-cooling. The mixture

was stirred at room temperature for 12 hours. To this reaction mixture were successively added ice water (50 ml) and a saturated aqueous sodium hydrogencarbonate solution (50 ml), and the mixture was extracted twice with ethyl acetate (200 ml). The organic layers were combined, washed with saturated brine (200 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography (n-hexane/ethyl acetate=5/1-2/1) to give (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)acrylamide (8.61 g, 100%) as a colorless solid. This was further purified by recrystallization from ethyl acetate to give colorless crystals (6.28 g, 81.9%).

The properties of this compound are shown in Table 15.

Examples 1-2 to 1-33

In the same manner as in the above Example 1-1, the compounds shown in Tables 15-25 were obtained.

Example 1-34

In the same manner as in Example 1-1 using 3-(4-methoxy-3-pentylthiophenyl)cinnamic acid (100 mg, 0.357 mmol) obtained in Preparative Example 103, N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)acrylamide (118 mg, 83%) was obtained as colorless crystals.

Example 1-35

In the same manner as in Example 1-1 using 3-(4-methoxy-3-pentylaminophenyl)cinnamic acid (100 mg, 0.380 mmol) obtained in Preparative Example 97, N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)acrylamide (31.1 mg, 21%) was obtained as pale-yellow crystals.

The properties of the compounds obtained in the above Example 1-34 and 1-35 are shown in Table 26.

Examples 1-36 to 1-92

In the same manner as in Example 1-1 to 1-35, the compounds of Example 1-36 to 1-92 were obtained. The properties of the compounds are shown in Tables 26-45.

Example 2-1

4-Methoxy-3-pentyloxybenzoic acid (4.77 g, 0.02 mol, 1 eq) and 1-hydroxybenzotriazole hydrate (2.7 g, 0.024 mol, 1.0 eq) were dissolved in DMF (50 ml), and to this solution were successively added 2-(4-hydroxyphenyl)ethylamine (4.1 g, 0.03 mol, 1.5 eq) and WSC hydrochloride (4.6 g, 0.024 mol, 1.2 eq) under ice-cooling. In the same manner as in Example 1-1, N-[2-(4-hydroxyphenyl)ethyl]-(4-methoxy-3-pentyloxy)benzamide (5.6 g, 79%) was obtained as colorless crystals.

The properties of this compound are shown in Table 46.

Examples 2-2 to 2-43

In the same manner as in the above Example 2-1, the compounds shown in Tables 46-60 were obtained.

Example 2-44

3,4-Dipentyloxy-[2-(4-nitrophenyl)ethyl]benzamide (110 mg, 0.25 mmol, 1.0 eq) was dissolved in methanol (11 ml), and 10% palladium-carbon catalyst (10 mg, water content 50%) was added. The mixture was stirred for 2 hours in a stream of hydrogen. The reaction mixture was cooled to room temperature, and filtered through Celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1) to give [2-(4-aminophenyl)ethyl]-3,4-dipentyloxybenzamide (94.1 mg, 91.7%) as colorless crystals.

Example 2-45

3,4-Dihexyloxybenzoic acid (161 mg, 0.5 mmol) and 1-hydroxybenzotriazole hydrate (45.9 mg, 0.3 mmol, 0.6 eq) were dissolved in DMF (5 ml), and to this solution were successively added 2-(4-hydroxyphenyl)ethylamine (82 mg, 0.6 mmol, 1.2 eq) and WSC hydrochloride (114 mg, 0.6 mmol, 1.2 eq) at room temperature. The mixture was stirred at room temperature for 15 hours. This reaction mixture was poured into ethyl acetate (75 ml), washed with water (5 ml x 3) and saturated brine (15 ml). The organic layer was dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (chloroform/methanol=50/1) to give 3,4-dihexyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide (230 mg). The obtained solid

was recrystallized from ethyl acetate-hexane to give 3,4-dihexyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide (194 mg, 88%) as colorless crystals.

Example 2-46

In the same manner as in Example 2-1 using 2-amino-4-methoxy-3-pentyloxybenzoic acid (45.0 g, 177.6 mmol) obtained in Preparative Example 79, 2-amino-4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide (67.85 g, 95%) was obtained as pale-yellow crystals.

Example 2-47

In the same manner as in Example 2-1 using 4-methoxy-2-nitro-3-pentyloxybenzoic acid (500 mg, 1.76 mmol) obtained in Preparative Example 78, 4-methoxy-2-nitro-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide (738 mg, 97%) was obtained as colorless crystals.

Example 2-48

4-Methoxy-2-nitro-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide obtained in Example 2-47, THF (1 ml) and sodium hydride (13.3 mg, 0.556 mmol) were mixed, and the mixture was stirred for 5 minutes. Ethyl bromoacetate (0.0617 ml, 0.556 mmol) was added, and the mixture was stirred at 90°C for 5.5 hours. Then, sodium hydride (6.7 mg, 0.278 mmol) and ethyl bromoacetate (6.7 mg, 0.278 mmol) were further added, and the mixture was stirred at 90°C for 6.5 hours. To the mixture was added water (3 ml) to stop the reaction, and the organic layer was extracted 3 times with ethyl acetate (5 ml). The organic layers were combined and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 4/1 - 2/3) to give ethyl{(4-methoxy-2-nitro-3-pentyloxybenzoyl)-[2-(4-nitrophenyl)ethyl]amino}acetate (0.137 g, 68%) as a pale-yellow oil.

Example 2-49

In the same manner as in Example 2-1 using 4-methoxy-2-methylthio-methyl-3-pentylaminobenzoic acid (90 mg, 0.30 mmol) obtained in Preparative Example 82, N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-2-methylthiomethyl-3-pentylamino-benzamide (113 mg, 90%) was obtained as colorless crystals.

Example 2-50

In the same manner as in Example 2-1 using 4-methoxy-2-methylthio-3-pentyloxybenzoic acid obtained in Preparative Example 83, N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-2-methylthio-3-pentyloxybenzamide was obtained as colorless crystals.

Example 2-51

In the same manner as in Example 2-1 using 2-ethoxycarbonylmethyl-4-methoxy-3-pentyloxybenzoic acid (45.01 g, 138.8 mmol) obtained in Preparative Example 90, ethyl{3-methoxy-2-pentyloxy-6-[2-(pyridin-4-yl)ethylcarbamoyl]-phenyl}acetate was obtained as a crude product. This product was used in the next reaction.

Example 2-52

In the same manner as in Example 2-1 using 4-pentyloxy-3-pentylthiobenzoic acid obtained in Preparative Example 112, N-[2-(4-amino-phenyl)ethyl]-4-pentyloxy-3-pentylthiobenzamide was obtained as colorless crystals.

The properties of the compounds obtained in the above Examples 2-44 to 2-52 are shown in Tables 60-63.

Examples 2-53 to 2-161

In the same manner as in Examples 2-1 to 2-52, the compounds of Examples 2-53 to 2-161 were obtained. The properties of the compounds are shown in Tables 63-99.

Example 3-1

4-Methoxy-3-pentyloxycinnamic acid (529 mg, 2.0 mmol, 1 eq) was dissolved in pyridine (10 ml), and to this solution were successively added 2-(4-hydroxyphenyl)ethyl alcohol (484 mg, 3.5 mmol, 1.5 eq) and WSC hydrochloride (460 mg, 2.4 mmol, 1.2 eq) under ice-cooling. In the same manner as in Example 1-1, 2-(4-hydroxyphenyl)ethyl-3-(4-methoxy-3-pentyloxy)cinnamate (61 mg, 7.9%) was obtained as colorless crystals.

The properties of this compound are shown in Table 100.

Examples 3-2 to 3-3

In the same manner as in the above Example 3-1, the compounds of Example 3-2 and 3-3 were obtained. The properties of the compounds are shown in Table

100.

Example 4-1

3-(1-Bromo-4-pentyloxynaphthalen-2-yl)cinnamic acid (51.2 mg, 0.141 mmol) and 1-hydroxybenzotriazole hydrate (19.1 mg, 0.141 mmol) were dissolved in DMF (1 ml), and to this solution were successively added 2-(4-hydroxyphenyl)-ethylamine (23.2 mg, 0.169 mmol) and WSC hydrochloride (32.4 mg, 0.169 mmol) under ice-cooling. In the same manner as in Example 1-1, (E)-3-(1-bromo-4-pentyloxynaphthalen-2-yl)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide (52.3 mg, 77%) was obtained as colorless crystals.

The properties of this compound are shown in Table 101.

Examples 4-2 to 4-4

In the same manner as in the above Example 4-1, the compounds shown in Tables 101-102 were obtained.

Example 5-1

7-Methoxy-8-pentyloxyquinoline-3-carbamic acid (24 mg, 0.083 mmol), chloroform (1.0 ml) and DMF (0.3 ml) were mixed, and to this solution were successively added a DMF solution (0.1 ml) of 2-(4-pyridinyl)ethylamine (12.2 mg, 0.1 mmol), WSC hydrochloride (19.2 mg, 0.1 mmol), and dimethylaminopyridine (1 mg, 0.0082 mmol). In the same manner as in Example 1-1, 7-methoxy-8-pentyloxyquinoline-3-carbamic acid (2-pyridin-4-ylethyl)amide (11.4 mg, 35%) was obtained as colorless crystals.

The properties of this compound are shown in Table 103.

Examples 5-2 to 5-9

In the same manner as in the above Example 5-1, the compounds of Example 5-2 to 5-9 were obtained. The properties of the compounds are shown in Tables 103-105.

Example 6-1

(1) 4-Methoxy-3-pentyloxybenzoic acid (5.96 g, 0.025 mol, 1 eq) was dissolved in thionyl chloride (7.3 ml, 0.100 mol, 4 eq), and the solution was stirred at room temperature for 24 hours. Excess thionyl chloride was evaporated under reduced pressure. Dichloromethane (10 ml) was added to the residue. 2-Amino-2-methylpropanol (5.01 ml, 0.053 mol, 2.1 eq) was added under ice-cooling, and the

mixture was stirred at room temperature for 2 hours. Water (200 ml) was added to this reaction mixture, and the mixture was extracted twice with ethyl acetate (200 ml). The organic layers were combined, washed with saturated brine (400 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=3/1-1/1) to give N-(2-hydroxy-1,1-dimethylethyl)-4-methoxy-3-pentyloxybenzamide (5.75 g, 74.4%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.38(1H, d, $J=2.1\text{Hz}$), 7.20(1H, dd, $J=8.3, 2.1\text{Hz}$), 6.84(1H, d, $J=8.3\text{Hz}$), 6.13(1H, bs), 4.79(1H, t, $J=6.1\text{Hz}$), 4.06(2H, t, $J=6.9\text{Hz}$), 3.90(3H, s), 3.69(2H, d, $J=6.1\text{Hz}$), 2.0-1.8(2H, m), 1.5-1.3(4H, m), 1.41(3H, s), 1.41(3H, s), 0.93(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 310 $[\text{M} + \text{H}^+]$ (100), 221(100), 238(50).

IR (Neat, cm^{-1}) : 3385, 2955, 1638, 1505.

(2) N-(2-Hydroxy-1,1-dimethylethyl)-4-methoxy-3-pentyloxybenzamide (5.498 g, 0.0178 mol, 1 eq) was dissolved in thionyl chloride (4.29 ml, 0.0214 mol, 3.3 eq), and the solution was stirred at room temperature for 1 hour. The reaction mixture was poured into diethyl ether (40 ml). The obtained hydrochloride compound was collected by filtration, and excess thionyl chloride was removed. A 1N aqueous sodium hydroxide solution (about 20 ml) was added to this hydrochloride compound under ice-cooling, whereby the mixture was alkalized ($\text{pH}=10$). The solution was extracted twice with diethyl ether (30 ml). The organic layers were combined, washed with saturated brine (60 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 2-(4-methoxy-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (4.46 g, 86%) as colorless crystals.

Example 6-2

2-(4-Methoxy-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (373 mg, 1.28 mmol, 1 eq) was dissolved in dimethoxyethane (7 ml). The solution was cooled to -60°C , and n-butyllithium (1.6 M hexane solution)(1.76 ml, 2.82 mmol, 2.2 eq) was added dropwise. The mixture was stirred at said temperature

for 1.5 hours. Ethylene oxide was added dropwise, and the mixture was stirred for 1.0 hour. The mixture was heated to room temperature, and further stirred for 2 hours. Water (50 ml) was added to the reaction mixture, and the mixture was extracted twice with ethyl acetate (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=3/1-2/1) to give [6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxyphenyl]ethanol (164 mg, 38.2%) as an oil.

Example 6-3

2-(4-Methoxy-3-pentyloxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (0.74 g, 2.54 mmol, 1 eq) was dissolved in dimethoxyethane (7 ml). The solution was cooled to -60°C, and n-butyllithium (1.6 M hexane solution)(3.5 ml, 5.59 mmol, 2.2 eq) was added dropwise. The mixture was stirred at said temperature for 1.5 hours. Ethyl chlorocarbonate was added dropwise, and the mixture was stirred for 1.0 hour. The mixture was heated to room temperature, and further stirred for 2 hours. Water (50 ml) was added to the reaction mixture, and the mixture was extracted twice with ethyl acetate (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=3/1) to give ethyl 6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxy benzoate (814 mg, 88.2%) as an oil.

Example 6-4

Lithium aluminum hydride (255 mg, 6.72 mol, 3.0 eq) was dissolved in THF (30 ml), and to this solution was added dropwise a THF solution (50 ml) of ethyl 6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxy benzoate (814 mg, 2.24 mmol, 1.0 eq) under ice-cooling. After the completion of the dropwise addition, the mixture was stirred at room temperature for 1.5 hours. This reaction mixture was cooled with ice-cold water, and a saturated aqueous sodium sulfate solution (about 20 ml) was added. After filtration through Celite, the filtrate was concentrated under reduced pressure. The obtained residue was

purified by column chromatography on silica gel (n-hexane/ethyl acetate=3/1) to give [6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxyphenyl]methanol (677 mg, 94.1%).

Example 6-5

2-[2-(4-Methoxy-3-pentyloxybenzoylamino)ethyl]pyridine N-oxide (200 mg, 0.558 mmol) was dissolved in acetic anhydride (2 ml), and the solution was stirred at 100°C for 30 minutes. This reaction mixture was concentrated under reduced pressure, and the obtained residue was subjected to column chromatography on silica gel (n-hexane/ethyl acetate=1/1) to give 2-[2-(4-methoxy-3-pentyloxyphenyl)-4,5-dihydrooxazol-5-yl]pyridine (①, 14.8 mg), and 163.5 mg of a mixture of N-(2-acetoxy-2-pyridin-2-ylethyl)-4-methoxy-3-pentyloxybenzamide (②) and N-[2-(5-acetoxypyridin-2-yl)ethyl]-4-methoxy-3-pentyloxybenzamide (③). ① was further purified by preparative thin layer chromatography to give a colorless oil (11.6 mg, 6.1%). The mixture of ② and ③ was separated and purified by preparative HPLC (ethyl acetate only, recycled) [② 95.7 mg, 42.7%, ③ 12.4 mg, 5.5%].

② : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.64-8.59(1H, m), 7.73(1H, td, $J=7.7$, 1.8Hz), 7.45-7.40(2H, m), 7.30-7.23(2H, m), 6.96(1H, t), 6.87(1H, d, $J=8.5\text{Hz}$), 6.03(1H, t, $J=5.7\text{Hz}$), 4.16-4.02(4H, m), 3.90(3H, s), 2.15(3H, s), 1.91-1.82(2H, m), 1.50-1.36(4H, m), 0.93(3H, t, $J=7.0\text{Hz}$).

FABMS (+) (m/z) : 402[M + 1] (26), 401(93), 341(67), 221(100).

③ : $^1\text{H-NMR}$ (CDCl_3 , 300MHz) δ :

8.40-8.32(1H, m), 7.43-7.40(2H, m), 7.27-7.22(2H, m), 6.85(1H, d, $J=8.4\text{Hz}$), 4.06(2H, t, $J=7.8\text{Hz}$), 3.89(3H, s), 3.84(2H, q, $J=5.9\text{Hz}$), 3.10(2H, t, $J=6.3\text{Hz}$), 2.34(3H, s), 1.91-1.80(2H, m), 1.49-1.33(4H, m), 0.93(3H, t, $J=7.0\text{Hz}$).

FABMS (+) (m/z) : 401[M + 1] (82), 221(73), 154(100).

Example 6-6

2-(3-Bromo-4-methoxyphenyl)-4,4-dimethyl-4,5-dihydrooxazole (400 mg, 1.41 mmol) obtained in the same manner as in Example 6-1 and THF (4 ml) were mixed, and this solution was cooled to -60°C. n-Butyllithium (1.6M hexane

solution, 1.94 ml, 3.1 mmol) was added and the mixture was stirred for 1.5 hours. Di-n-amyldisulfide (0.69 ml, 3.1 mmol) was added to this reaction mixture, and the mixture was stirred for 4 hours at room temperature. To the mixture was added 1N hydrochloric acid (2 ml), and the aqueous layer was extracted 3 times with ethyl acetate (5 ml). The organic layer was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 4/1) to give 2-(4-methoxy-3-pentylthiophenyl)-4,4-dimethyl-4,5-dihydrooxazole (422 mg, 97%) as a colorless oil.

The properties of the compounds obtained in the above Example 6-1 to 6-6 are shown in Tables 106 and 107.

Examples 6-7 to 6-13

In the same manner as in Examples 6-1 to 6-6, the compounds of Examples 6-7 to 6-13 were obtained. The properties of the compounds are shown in Tables 108-110.

Example 7-1

3-Nitrophthalic anhydride (1.93 g, 0.01 mol, 1 eq) and 2-(4-hydroxyphenyl)-ethylamine (2.06 g, 0.015 mol, 1.5 eq) were refluxed under heating in toluene (20 ml) for 3 hours. The reaction mixture was cooled to room temperature, and ethyl acetate (100 ml) was added to this reaction mixture. The organic layer was washed twice with dil. aqueous hydrochloric acid solution (30 ml), further washed with saturated brine (100 ml), and dried over anhydrous sodium sulfate. After the drying agent was filtered off, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=1/1) to give N-[2-(4-hydroxyphenyl)ethyl]-3-nitrophthalimide (2.92 g, 92.8%) as a colorless solid. This was further purified by recrystallization from methanol to give colorless crystals (1.9 g, 60.8%).

Example 7-2

10% Palladium-carbon catalyst (water content 50%, 200 mg) was added to a mixed solution of N-[2-(4-hydroxyphenyl)ethyl]-3-nitrophthalimide (1.67 g, 0.0053 mol, 1 eq) in methanol (20 ml)-ethanol (50 ml)-acetic acid (20 ml), and the mixture was stirred for 3 hours at room temperature in a stream of hydrogen. The

reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (chloroform/methanol=50/1) to give 3-amino-N-[2-(4-hydroxyphenyl)ethyl]phthalimide (360 mg, 24.1%) as a colorless solid.

Example 7-3

3-Amino-N-[2-(4-hydroxyphenyl)ethyl]phthalimide (110 mg, 0.390 mmol, 1 eq) was dissolved in acetone (30 ml), and to this solution were added 1-chloro-1-pentanone (70.5 mg, 0.585 mmol, 1.5 eq) and triethylamine (0.081 ml, 0.585 mmol, 1.5 eq) in this order. The mixture was refluxed under heating for 30 minutes. This reaction mixture was cooled to room temperature. Ice water (10 ml) and citric acid (10 ml) were added, and the mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (30 ml) and dried over anhydrous sodium sulfate. After the drying agent was filtered off, the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=5/1) to give 4-[2-(1,3-dioxo-4-pentanoylamino-1,3-dihydroisoindol-2-yl)ethyl]phenyl pentanoate (80.2 mg, 56.2%) as colorless crystals.

Example 7-4

(1) Ethyl 6-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxybenzoate (200 mg, 0.55 mmol, 1 eq) was dissolved in a 3N aqueous hydrochloric acid solution (20 ml), and the solution was refluxed under heating for 11 hours. After the completion of the reaction, the mixture was cooled to room temperature and extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (40 ml) and dried over anhydrous sodium sulfate. After the drying agent was filtered off, the filtrate was concentrated under reduced pressure. The obtained residue was dissolved in a 1N aqueous potassium hydroxide solution (10 ml), and the mixture was stirred for 1.5 hours at room temperature. Ice water and a 3N aqueous hydrochloric acid solution (30 ml) were added to the reaction mixture to make the same acidic. The mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (40 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced

pressure to give 4-methoxy-3-pentyloxyphthalic acid (178 mg, 100%).

(2) 2-Methoxy-3-pentyloxyphthalic acid (155 mg, 0.55 mmol, 1 eq) and 2-(4-hydroxyphenyl)ethylamine (101.6 mg, 0.74 mmol, 1.4 eq) were dissolved in acetic acid (10 ml), and the solution was refluxed under heating for 2 hours. The mixture was cooled to room temperature and extracted twice with ethyl acetate (40 ml). The organic layers were combined, washed with a 1N aqueous hydrochloric acid solution (40 ml) and further with saturated brine (40 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure and purified by column chromatography on silica gel (n-hexane/ethyl acetate=4/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentyloxyisoindole-1,3-dione (67 mg, 31.8%).

Example 7-5

[6-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxy-phenyl]methanol (344 mg, 1.07 mmol, 1.0 eq) was dissolved in DMSO (4 ml), and triethylamine (1.4 ml, 9.63 mmol, 9.0 eq) was added to this solution. The mixture was cooled with cold water. Sulfur trioxide-pyridine complex (511 mg, 3.21 mmol, 3.0 eq) was added, and the mixture was stirred at room temperature for 1.5 hours. Water (5 ml) was added to this reaction mixture, and the mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (200 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was dissolved in methanol (16 ml), and 2-(4-hydroxyphenyl)ethylamine (146.8 mg, 1.07 mmol, 1.0 eq) and cyanoborohydride (67.3 mg, 1.07 mmol, 1.0 eq) were added. The mixture was stirred at room temperature for 10 hours. The reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel (n-hexane/ethyl acetate=5/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (6.7 mg, 1.7%).

Example 7-6

3-Hydroxyphthalic anhydride (1.0 g, 6.6 mmol) was dissolved in methanol (20 ml), and a catalytic amount of p-toluene sulfonic acid was added to this solution. The mixture was stirred with refluxing under heating for 5 hours, and

concentrated under reduced pressure to give a crude product of dimethyl 3-hydroxyphthalate. The crude product of dimethyl 3-hydroxyphthalate was dissolved in DMF (20 ml), and potassium carbonate (6 g, 43 mmol) and n-amy bromide (3 ml, 24 mmol) were added to this solution. The mixture was stirred at 90°C for 1.5 hours, and solids were removed by filtration through Celite. The filtrate was concentrated under reduced pressure to give a crude product of dimethyl 3-pentyloxyphthalate. The crude product of dimethyl 3-pentyloxyphthalate was dissolved in methanol (10 ml), and a 1N aqueous sodium hydroxide solution (20 ml) was added to this solution. The mixture was stirred at 90°C for 2 hours, and a 3N aqueous hydrochloric acid solution (15 ml) was added to the reaction mixture. The mixture was extracted with ethyl acetate (30 ml x 3), and washed with saturated brine (20 ml). The organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of 3-pentyloxyphthalic acid. The crude product of 3-pentyloxyphthalic acid was dissolved in acetic acid (20 ml), and tyramine hydrochloride (1.0 g, 7.3 mmol) was added. The mixture was stirred at 90°C for 2 hours and concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=4/1) to give N-2-(4-hydroxyphenyl)ethyl-3-pentyloxyphthalimide (0.8 g, 2.3 mmol, 35%) as colorless crystals.

Example 7-7

N-2-(4-Hydroxyphenyl)ethyl-3-pentyloxyphthalimide (412 mg, 1.17 mmol) was dissolved in THF (1 ml), and a 1.0M THF solution (4 ml) of $\text{BH}_3 \cdot \text{THF}$ (4.0 mmol) was added to this solution. The mixture was stirred with refluxing under heating for 8 hours. A 3N aqueous hydrochloric acid solution (10 ml) was added to the reaction mixture. The mixture was further stirred for 0.5 hour at the same temperature, and water (20 ml) was added. The mixture was extracted with ethyl acetate (20 ml x 3), and washed with a saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (30 ml). The organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl

acetate=2/1) to give N-2-(4-hydroxyphenyl)ethyl-7-pentyloxyisoindol-1-one (232 mg, 0.68 mmol, 59%) as colorless crystals.

Example 7-8

A suspension of lithium aluminum hydride (LAH, 74 mg, 2 mmol) in THF (1 ml) was added to a solution of N-2-(4-hydroxyphenyl)ethyl-3-pentyloxyphthalimide (351 mg, 0.99 mmol) in THF (1 ml) at 0°C. The mixture was stirred at room temperature for 5 hours. This reaction mixture was poured into a 3N aqueous hydrochloric acid solution (20 ml). The mixture was extracted with ethyl acetate (20 ml x 3), and washed with a saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (30 ml). The organic layer was combined, and dried over anhydrous magnesium sulfate. The drying agent was filtered off, the filtrate was concentrated under reduced pressure and the obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=2/1) to give N-2-(4-hydroxyphenyl)ethyl-3-pentyloxyisoindoline (130 mg, 40%) as colorless crystals.

Example 7-9

(1) Dimethyl 4-hydroxyphthalate (10.0 g, 47 mmol) was dissolved in DMF (100 ml), and potassium carbonate (30 g, 217 mmol) and n-amy bromide (10 ml, 80 mmol) were added to this solution. The mixture was stirred at 90°C for 2 hours, and the solid was removed by filtration through Celite. The filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=4/1) to give dimethyl 4-pentyloxyphthalate (12.7 g, 45.4 mmol, 97%) as a colorless oil.

¹H-NMR (CDCl₃, 300MHz) δ : 7.80(1H, d, J=8.40Hz),

7.05(1H, d, J=2.70Hz), 6.97(1H, dd, J=8.40, 2.70Hz),

4.00(2H, t, J=6.90Hz), 3.91(3H, s), 3.87(3H, s),

1.80(2H, quint, J=6.98Hz), 1.47-1.34(4H, m), 0.93(3H, t, J=7.20Hz).

FABMS (+) (m/z) : 281[M + 1] (42), 249(100), 179(78).

(2) Dimethyl 4-pentyloxyphthalate (3.0 g, 10.7 mmol) was dissolved in methanol (20 ml), and a 1N aqueous sodium hydroxide solution (25 ml) was added to this solution. The mixture was stirred at room temperature for 6.5 hours. A 3N aqueous hydrochloric acid solution (20 ml) was added to this reaction mixture.

The mixture was extracted with ethyl acetate (40 ml×3), and washed with saturated brine (30 ml). The organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give a crude product of 4-pentyloxyphthalic acid.

This crude product was not further purified, but used in the next reaction.

The crude product of 4-pentyloxyphthalic acid was dissolved in acetic acid (20 ml), and tyramine hydrochloride (2.74 g, 20 mmol) was added. The mixture was stirred at 96°C for 4 hours, and concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=6/1) to give N-2-(4-hydroxyphenyl)ethyl-4-pentyloxyphthalimide (2.6 g, 9.4 mmol, 88%) as colorless crystals.

Example 7-10

N-2-(4-Hydroxyphenyl)ethyl-4-pentyloxyphthalimide (330 mg, 0.93 mmol) was dissolved in THF (1 ml), and a 1.0M THF solution (1.5 ml) of $\text{BH}_3 \cdot \text{THF}$ (1.5 mmol) was added to this solution. The mixture was stirred with refluxing under heating for 1.5 hours. A 3N aqueous hydrochloric acid solution (2 ml) was added to this reaction mixture. The mixture was further stirred for 0.5 hour at the same temperature, and water (20 ml) was added. The mixture was extracted with ethyl acetate (20 ml×3), and washed with a saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (30 ml). The organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate=2/1) to give N-2-(4-hydroxyphenyl)ethyl-4-pentyloxyisoindol-1-one (①) (139 mg, 0.41 mmol, 44%, colorless crystals) and N-2-(4-hydroxyphenyl)ethyl-5-pentyloxyisoindol-1-one (②) (111 mg, 0.33 mmol, 35%, colorless crystals).

Example 7-11

A suspension of LAH (40 mg, 1.1 mmol) in THF (1 ml) was added to a solution of N-2-(4-hydroxyphenyl)ethyl-4-pentyloxyphthalimide (208 mg, 0.59 mmol) in THF (1 ml) at 0°C. The mixture was stirred at room temperature for 3.5 hours. This reaction mixture was poured into a 3N aqueous hydrochloric acid solution (20 ml). The mixture was extracted with ethyl acetate (20 ml×3), and washed with a

saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (30 ml). The organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (chloroform/methanol=30/1) to give N-2-(4-hydroxyphenyl)ethyl-4-pentyloxyisindoline (181 mg, 94%) as colorless crystals.

Example 7-12

(1) [6-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxyphenyl]-methanol (4.69 g, 0.014 mmol, 1 eq) was dissolved in 3N hydrochloric acid (50 ml), and the solution was stirred under heating for 3 hours. After the completion of the reaction, the mixture was cooled to room temperature and extracted twice with diethyl ether (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=2/1) to give 5-methoxy-4-pentyloxy-3H-isobenzofuran-1-one (3.4 g, 82.4%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.61(1H, d, $J=8.3\text{Hz}$),
7.07(1H, d, $J=8.3\text{Hz}$), 5.28(2H, s), 4.09(2H, t, $J=6.6\text{Hz}$), 3.95(3H, s),
1.8-1.7(2H, m), 1.5-1.3(4H, m), 0.93(3H, t, $J=6.9\text{Hz}$).

FABMS (m/z) : 251 [$\text{M} + \text{H}^+$] (100).

(2) 2-(4-Benzoyloxyphenyl)ethylamine (377 mg, 1.66 mmol, 2 eq) was dissolved in dichloromethane (3 ml), and trimethylaluminum (15% hexane solution, 0.88 ml, 1.825 mmol, 2.2 eq) was added. The mixture was stirred for 30 minutes. A dichloromethane solution (3 ml) of 5-methoxy-4-pentyloxy-3H-isobenzofuran-1-one (207.6 mg, 0.83 mmol, 1 eq) was added dropwise thereto, and the mixture was stirred for 24 hours. 3N Hydrochloric acid (20 ml) was added to this solution, and the mixture was extracted 3 times with chloroform (10 ml). The organic layers were combined, washed with saturated brine (50 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=2/1-1/1) to give 2-

(2-hydroxymethyl)-4-methoxy-3-pentyloxy-N-[2-(4-benzyloxyphenyl)-ethyl]benzamide (204 mg, 51.5%) as colorless crystals.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.3(5H, m), 7.15(2H, d, $J=8.5\text{Hz}$), 7.11(1H, d, $J=8.5\text{Hz}$), 6.93(2H, d, $J=8.5\text{Hz}$), 6.79(1H, d, $J=8.5\text{Hz}$), 6.20(1H, t, $J=6.7\text{Hz}$), 5.05(2H, s), 4.65(2H, d, $J=6.7\text{Hz}$), 4.20(1H, t, $J=6.7\text{Hz}$), 3.97(2H, t, $J=6.7\text{Hz}$), 3.85(3H, s), 3.67(2H, q, $J=6.8\text{Hz}$), 2.88(2H, t, $J=6.8\text{Hz}$), 1.9-1.7(2H, m), 1.5-1.3(4H, m), 0.93(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 478 [$\text{M} + \text{H}^+$] (30), 460(100).

IR (KBr , cm^{-1}) : 3333, 2937, 1623, 1510, 1268, 1216, 1014.

Elemental analysis : $\text{C}_{29}\text{H}_{35}\text{NO}_5$

Calculated C 72.93, H 7.39, N 2.93

Found C 73.06, H 7.50, N 2.79

Example 7-13

2-(2-Hydroxymethyl)-4-methoxy-3-pentyloxy-N-[2-(4-benzyloxyphenyl)ethyl]benzamide (219.1 mg, 0.459 mmol, 1.0 eq) was dissolved in DMSO (3 ml), and triethylamine (0.59 ml, 4.13 mmol, 9 eq) and sulfur trioxide-pyridine complex (219 mg, 1.38 mmol, 3 eq) were added under ice-cooling. The mixture was stirred at room temperature for 4 hours. A saturated aqueous sodium hydrogencarbonate solution (10 ml) was added to this reaction mixture, and the mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (30 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=3/1) to give 2-[2-(4-benzyloxyphenyl)ethyl]-3-hydroxy-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (163 mg, 74.7%) as a colorless oil.

Example 7-14

2-[2-(4-Benzyloxyphenyl)ethyl]-3-hydroxy-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (142 mg, 0.30 mmol, 1.0 eq) was dissolved in dichloromethane (3 ml), and triethylsilane (0.095 ml, 0.60 mmol, 2.0 eq) was added. The mixture was stirred for 10 minutes at room temperature.

Trifluoroacetic acid was added thereto, and the mixture was further stirred for 4 hours. A saturated aqueous sodium hydrogencarbonate solution (30 ml) was added to this reaction mixture. The mixture was extracted twice with ethyl acetate (30 ml). The organic layers were combined, then washed with saturated brine (60 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 2-[2-(4-benzyloxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (136 mg, 99.8%) as a colorless oil.

Example 7-15

2-[2-(4-Benzyloxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (125.9 mg, 0.274 mmol, 1.0 eq) was dissolved in ethyl acetate (10 ml), and 10% palladium-carbon catalyst (80 mg, water content 50%) was added. The mixture was stirred in a stream of hydrogen for 3 hours. After the completion of the reaction, the mixture was filtered through Celite and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one (75 mg, 74.1%) as colorless crystals.

This compound and the compound of Example 7-5 are the same, and have the same properties.

Example 7-16

(1) [6-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)-3-methoxy-2-pentyloxyphenyl]-ethanol (4.69 g, 0.014 mmol, 1 eq) was dissolved in 3N hydrochloric acid (50 ml), and the solution was stirred under heating for 1.5 hours. The mixture was cooled to room temperature, and an aqueous sodium hydroxide solution was added under ice-cooling to make same alkaline (pH=13-14). The mixture was stirred for 1 hour at room temperature. Hydrochloric acid was added to this solution and the mixture was made acidic (pH=1-2). This mixture was extracted twice with diethyl ether (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-

hexane/ethyl acetate=2/1) to give 6-methoxy-5-pentyloxy-3,4-dihydroisocoumalin (3.36 g, 90.2%) as a colorless oil.

$^1\text{H-NMR}$ (CDCl_3) δ : 7.86(1H, d, $J=8.6\text{Hz}$),
6.92(1H, d, $J=8.6\text{Hz}$), 4.48(2H, t, $J=6.0\text{Hz}$), 3.95(2H, t, $J=6.8\text{Hz}$),
3.92(3H, s), 3.06(2H, t, $J=6.0\text{Hz}$), 1.8-1.7(2H, m), 1.5-1.3(4H, m),
0.93(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 265 $[\text{M} + \text{H}^+]$ (100).

(2) A solution (2 ml) of 2-(4-benzyloxyphenyl)ethylamine (1.15 g, 5.1 mmol, 1 eq) in dichloromethane was dissolved in dichloromethane (30 ml), and trimethylaluminum (15% hexane solution, 4.9 ml, 10.2 mmol, 2 eq) was added dropwise. The mixture was stirred at room temperature for 30 minutes. A dichloromethane solution (30 ml) of 6-methoxy-5-pentyloxy-3,4-dihydroisocoumalin (1.36 g, 5.1 mol, 1 eq) was added dropwise thereto, and the mixture was stirred at room temperature for 12 hours. 3N Hydrochloric acid (20 ml) was added to this solution, and the mixture was extracted twice with dichloromethane (20 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=1/1-ethyl acetate) to give 2-(2-hydroxyethyl)-4-methoxy-3-pentyloxy-N-[2-(4-benzyloxyphenyl)ethyl]benzamide (1.35 g, 53.7%) as colorless crystals.

m.p. : 93.4-93.7°C

$^1\text{H-NMR}$ (CDCl_3) δ : 7.5-7.3(5H, m), 7.15(2H, d, $J=8.6\text{Hz}$),
7.05(1H, d, $J=8.5\text{Hz}$), 6.93(2H, d, $J=8.6\text{Hz}$), 6.75(1H, d, $J=8.5\text{Hz}$),
6.40(1H, bs), 5.05(2H, s), 3.96(1H, bs), 3.94(2H, t, $J=6.7\text{Hz}$),
3.86(2H, q, $J=5.7\text{Hz}$), 3.84(3H, s), 3.65(2H, q, $J=6.8\text{Hz}$),
2.94(2H, t, $J=5.7\text{Hz}$), 2.86(2H, t, $J=6.8\text{Hz}$), 1.8-1.7(2H, m),
1.5-1.3(4H, m), 0.92(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 492 $[\text{M} + \text{H}^+]$ (100), 210(60).

IR (KBr, cm^{-1}) : 3291, 2932, 1614, 1512, 1243.

Elemental analysis : $\text{C}_{30}\text{H}_{37}\text{NO}_5$

Calculated C 73.29, H 7.59, N 2.85

Found C 73.51, H 7.72, N 2.80

Example 7-17

2-(2-Hydroxyethyl)-4-methoxy-3-pentyloxy-N-[2-(4-benzyloxyphenyl)-ethyl]benzamide (1.33 g, 2.7 mmol, 1.0 eq) was dissolved in DMSO (26 ml), and triethylamine (3.49 ml, 24.3 mmol, 9 eq) and sulfur trioxide-pyridine complex (1.29 g, 8.1 mmol, 3 eq) were successively added under ice-cooling. The mixture was stirred at room temperature for 2 hours. 3N Hydrochloric acid (35 ml) was added to this reaction mixture. The mixture was stirred at room temperature for 30 minutes and extracted twice with ethyl acetate (40 ml). The organic layers were combined, washed with a saturated aqueous sodium carbonate solution (40 ml) and saturated brine (100 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=2/1) to give 2-[2-(4-benzyloxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (1.275 g, 100%) as colorless crystals.

Example 7-18

10% Palladium hydroxide - carbon catalyst (300 mg, water content 50%) was added to a solution of 2-[2-(4-benzyloxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (1.18 g, 2.5 mmol, 1.0 eq) in acetic acid (20 ml), and the mixture was stirred with heating in a stream of hydrogen for 4 hours at 60-70°C at 3 kgf/cm². The reaction mixture was cooled to room temperature, and filtered through Celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=4/1) to give 6-methoxy-2-[2-(4-oxocyclohexyl)ethyl]-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (800 mg, 82.6%) as a pale-yellow oil.

Example 7-19

2-(2-Hydroxyethyl)-4-methoxy-3-pentyloxy-N-[2-(4-hydroxyphenyl)-ethyl]benzamide (121.9 mg, 0.304 mmol, 1.0 eq) was dissolved in DMSO (6 ml), and triethylamine (0.39 ml, 2.7 mmol, 9 eq) and sulfur trioxide-pyridine complex (145 mg, 0.91 mmol, 3 eq) were successively added under ice-cooling. The mixture was stirred at room temperature for 2 hours. Water (20 ml) and a saturated aqueous sodium hydrogencarbonate solution (10 ml) were successively

added to the reaction mixture, and the mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed successively with a saturated aqueous ammonium chloride solution (40 ml) and saturated brine (40 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=3/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (①) (59 mg, 20.3%) as colorless crystals and 3-hydroxy-2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (②) (103.1 mg, 82.5%) as a colorless oil.

② : $^1\text{H-NMR}$ (CDCl_3) δ : 7.85(1H, d, $J=8.7\text{Hz}$), 7.09(2H, d, $J=8.5\text{Hz}$), 6.89(1H, d, $J=8.7\text{Hz}$), 6.77(2H, d, $J=8.5\text{Hz}$), 5.50(1H, bs), 4.82(1H, m), 4.1-4.0(1H, m), 4.0-3.9(2H, m), 3.88(3H, s), 3.7-3.5(1H, m), 3.3-3.2(1H, m), 3.0-2.8(3H, m), 2.3-2.2(1H, bs), 1.8-1.7(2H, m), 1.5-1.3(4H, m), 0.92(3H, t, $J=7.1\text{Hz}$).

FABMS (m/z) : 400 [$\text{M} + \text{H}^+$] (80), 382(60).

IR (Neat, cm^{-1}) : 3304, 2934, 1631, 1597, 1468, 1281.

Example 7-20

2-(2-Hydroxyethyl)-4-methoxy-3-pentyloxy-N-(2-pyridin-4-ylethyl)-benzamide (90 mg, 233 μmol , 1.0 eq) was dissolved in DMSO (2 ml), and triethylamine (0.3 ml, 2.10 mmol, 9 eq) and sulfur trioxide-pyridine complex (111.2 mg, 0.70 mmol, 3 eq) were successively added under ice-cooling. The mixture was stirred at room temperature for 4 hours. 3N Hydrochloric acid (15 ml) was added to this reaction mixture, and the mixture was stirred at room temperature for 1 hour. Sodium hydroxide was added to make the same alkaline. The solution was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (40 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate) and recrystallized from ethyl acetate to give 2-[2-(4-pyridyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (40.2 mg, 47.1%) as colorless crystals.

Example 7-21

2-[2-(4-Benzoyloxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (1.21 g, 2.6 mmol, 1.0 eq) was dissolved in ethyl acetate (12 ml), and 10% palladium-carbon catalyst (300 mg, water content 50%) was added. The mixture was stirred in a stream of hydrogen for 4 hours. The reaction mixture was cooled to room temperature and filtered through Celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1-ethyl acetate) to give 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (681.8 mg, 68.7%) as colorless crystals.

This compound and the compound of Example 7-19 ① are the same, and have the same properties.

Example 7-22

2-[2-(4-Hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one (681.8 mg, 1.79 mmol, 1.0 eq) was dissolved in dichloromethane (7 ml), and 2,6-lutidine (575 mg, 5.36 mmol, 3 eq) and acetic anhydride (1.13 g, 5.36 mmol, 3 eq) were successively added under ice-cooling. The mixture was stirred at room temperature for 12 hours and refluxed under heating for 3 hours. The reaction mixture was cooled to room temperature, and water (10 ml) and a 10% aqueous hydrochloric acid solution (10 ml) were successively added. The mixture was extracted twice with dichloromethane (30 ml). The organic layers were combined, washed with saturated brine (40 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1) to give 4-[2-(6-methoxy-1-oxo-5-pentyloxy-1H-isoquinolin-2-yl)ethyl]phenyl acetate (734 mg, 97.0%) as colorless crystals.

Example 7-23

4-[2-(6-Methoxy-1-oxo-5-pentyloxy-1H-isoquinolin-2-yl)ethyl]phenyl acetate (5.65 g, 13.0 mmol, 1.0 eq) was dissolved in acetic acid (60 ml), and 10% palladium-carbon catalyst (5.6 g, water content 50%) was added. The mixture was stirred with heating in a stream of hydrogen for 8 hours at 60-70°C at a pressure of 3 kgf/cm². The reaction mixture was cooled to room temperature and

filtered through Celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1) to give 4-[2-(6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)ethyl]phenylacetate (4.067 g, 73.5%) as colorless crystals.

Example 7-24

4-[2-(6-Methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)ethyl]phenyl acetate (720 mg, 1.69 mmol, 1 eq) was dissolved in methanol (10 ml), and aqueous ammonia (10 ml) was added. The mixture was stirred for 2 hours at room temperature. The reaction mixture was concentrated under reduced pressure, and water (20 ml) was added to the residue. The mixture was extracted twice with ethyl acetate (30 ml). The organic layers were combined, washed with a 1N aqueous hydrochloric acid solution (10 ml) and saturated brine (50 ml), and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate/hexane=1/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (396 mg, 61.0%) as colorless crystals.

Example 7-25

4-[2-(6-Methoxy-1-oxo-7-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)ethyl]phenyl acetate (25 mg, 0.0588 mmol, 1.0 eq) was dissolved in methanol (1 ml), and aqueous ammonia (3 drops) was added. The mixture was stirred for 1 hour at room temperature. The reaction mixture was concentrated under reduced pressure to give a colorless solid (21 mg, 93.1%). This was purified by recrystallization from a mixed solution of ethyl acetate and methanol to give 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-7-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (15 mg, 66.5%) as colorless needles.

Example 7-26

4-{2-[(2-Acetoxy-2-benzenesulfanylethyl)-(4-methoxy-3-pentyloxybenzoyl-amino)]ethyl}phenyl acetate (1.575 g, 0.0027 mmol, 1 eq) was dissolved in benzene (15 ml), and trichloroacetic acid (3.65 g) was added. The mixture was refluxed under heating for 2 hours. The reaction mixture was made acidic with a 3N

aqueous hydrochloric acid solution (40 ml). The solution was extracted twice with dichloromethane (70 ml). The organic layers were combined, washed with saturated brine (140 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=1/1) to give 2-[2-(4-acetyloxyphenyl)ethyl]-(6-methoxy-7-pentyloxy)-2H-isoquinolin-1-one (500 mg, 43.7%) as a colorless solid.

Example 7-27

4-{2-[(2-Acetoxy-2-benzenesulfanylethyl)-(4-methoxy-3-pentyloxybenzoylamino)]ethyl}phenyl acetate (565 mg, 1.02 mmol) was dissolved in toluene (12 ml), and p-toluenesulfonic acid monohydrate (390 mg, 2.05 mol, 2 eq) was added. The mixture was refluxed with heating for 1 hour. A 1N aqueous potassium hydroxide solution (20 ml) was added under ice-cooling. The mixture was stirred at room temperature for 30 minutes. In the same manner as in Example 7-26, 2-[2-(4-hydroxyphenyl)ethyl]-(6-methoxy-7-pentyloxy)-2H-isoquinolin-1-one (287 mg, 74%) was obtained as colorless crystals.

Example 7-28

In the same manner as in Example 7-27 using 4-{2-[(2-acetoxy-2-benzenesulfanylethyl)-(3-methoxy-4-pentyloxybenzoylamino)]ethyl}phenyl acetate, 2-[2-(4-hydroxyphenyl)ethyl]-(7-methoxy-6-pentyloxy)-2H-isoquinolin-1-one (31 mg, 7.9%) was obtained as colorless crystals.

Example 7-29

10% Palladium-carbon catalyst (water content 50%, 100 mg) was added to a solution of 2-[2-(4-acetyloxyphenyl)ethyl]-(6-methoxy-7-pentyloxy)-2H-isoquinolin-1-one (300 mg, 0.708 mmol, 1.0 eq) in acetic acid (5 ml), and the mixture was stirred in a stream of hydrogen at room temperature under a pressure of 3 kgf/cm² for 16 hours. The reaction mixture was filtered through Celite, and the filtrate was concentrated under reduced pressure to give 4-[2-(6-methoxy-1-oxo-7-pentyloxy-3,4-dihydro-2H-isoquinolin-2-yl)ethyl]phenyl acetate (90 mg, 47.7%) as colorless crystals.

Example 7-30

4,5-Dipentyloxy-3-hydroxy-2-[2-(4-nitrophenyl)ethyl]-2,3-dihydroisoindol-1-

one (1.04 g, 2.2 mmol, 1.0 eq) was dissolved in dichloromethane (20 ml), and triethylsilane (0.70 ml, 4.4 mmol, 2.0 eq) was added. The mixture was stirred for 10 minutes at room temperature. Trifluoroacetic acid (2.2 ml) was added dropwise thereto, and the mixture was further stirred for 4 hours. A saturated aqueous sodium hydrogencarbonate solution (40 ml) was added to this reaction mixture, and the mixture was extracted 3 times with ethyl acetate (30 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure to give 4,5-dipentyloxy-2-[2-(4-nitrophenyl)ethyl]-2,3-dihydroisindol-1-one (868 mg, 86.8%) as pale-yellow crystals.

Example 7-31

N-[2-(4-Hydroxyphenyl)ethyl]-4-methoxy-2-methylthiomethyl-3-pentylaminobenzamide (93 mg, 0.223 mmol) obtained in Example 2-49, methylene chloride (1 ml) and molecular sieve 4A (100 mg) were mixed, and the mixture was cooled to 0°C. N-Chlorosuccinimide (44.7 mg, 0.33 mmol) was added, and the mixture was stirred at room temperature for 24 hours. Saturated brine (0.5 ml) was added to the mixture, and the aqueous layer was extracted 5 times with ethyl acetate (5 ml). The organic layers were combined, and dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified twice by column chromatography on silica gel (chloroform/methanol = 50/1 - 10/1, hexane/ethyl acetate = 1/2) to give 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentylamino-2,3-dihydroindol-1-one (12.4 mg, 15 %) as colorless crystals.

Example 7-32

N-[2-(4-Hydroxyphenyl)ethyl]-4-methoxy-2-methylthio-3-pentyloxy-benzamide (85 mg, 0.21 mmol) obtained in Example 2-50, molecular sieve 4A (200 mg) and methylene chloride (1 ml) were mixed, and this mixture was cooled to 0°C. N-Chlorosuccinimide (29.4 mg, 0.22 mmol) was added, and the mixture was stirred at room temperature for 5 hours. The reaction mixture was filtered, ethyl acetate (20 ml) was added to the filtrate, and the mixture was washed twice with

saturated brine (5 ml). The mixture was dried over anhydrous magnesium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified twice by column chromatography on silica gel (hexane/ethyl acetate = 1/1) to give a pale-yellow oil. To allow reaction of the residual raw materials, this oil, molecular sieve 4A (200 mg) and methylene chloride (1 ml) were mixed, and cooled to 0°C. N-Chlorosuccinimide (17.4 mg, 0.13 mmol) was added, and the reaction mixture was stirred at room temperature for 2 hours, followed by filtration. Ethyl acetate (20 ml) was added to the filtrate, and the filtrate was washed once with saturated brine (5 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by thin layer chromatography (chloroform/methanol = 20/1) to give 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-7-pentyloxybenzo[d]isothiazol-3-one (34 mg, 42%) as colorless crystals.

Example 7-33

2-(2-Hydroxymethyl)-3,4-bis(pentyloxy)-N-[2-(4-nitrophenyl)ethyl]benzamide (19.83 g, 42.0 mmol, 1.0 eq) obtained in Example 2-120 was dissolved in DMSO (200 ml), and sulfur trioxide-pyridine complex (20.1 g, 12.6 mmol, 3 eq) and triethylamine (52.7 g, 37.8 mmol, 9 eq) were successively added under cooling with cold water. The mixture was allowed to warm up to room temperature and the mixture was stirred at the same temperature for 2 hours. After addition of saturated sodium hydrogencarbonate solution (300 ml), the mixture was extracted with ethyl acetate (400 ml). The organic layer was washed with saturated brine (300 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give 3-hydroxy-2-[2-(4-nitrophenyl)ethyl]-4,5-bis(pentyloxy)-2,3-dihydroisoindol-1-one (32.2 g, over weight) as a yellow oil.

Example 7-34

4,5-Dipentyloxy-2-[2-(4-nitrophenyl)ethyl]-2,3-dihydroisoindol-1-one (19.69 g, 43.3 mmol, 1.0 eq) obtained in Example 7-30 was dissolved in ethanol (200 ml), and 5% palladium-carbon catalyst (3.8 g, water content 50%) was added. The reaction mixture was stirred in a stream of hydrogen at room temperature for 2.5

hours under the pressure of 3 kgf/cm², and filtered through celite. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (ethyl acetate/chloroform = 1/2) to give 2-[2-(4-aminophenyl)ethyl]-4,5-bis(pentyloxy)-2,3-dihydroisoindol-1-one (17.19 g, 93.5%) as pale-yellow crystals.

Example 7-35

2-[2-(4-Aminophenyl)ethyl]-4,5-bis(pentyloxy)-2,3-dihydroisoindol-1-one (22.37 g, 52.7 mmol, 1.0 eq) obtained in Example 7-34 was dissolved in methanol (100 ml), and 10% HCl- methanol solution (86.0 g, 236 mmol, 4.4 eq) was added to this solution. The mixture was stirred at room temperature for 30 minutes, and concentrated under reduced pressure to remove the solvent. The obtained residue was washed with hexane and dissolved in ethanol by heating. After cooling at room temperature for 1 hour, the mixture was stirred under ice-cooling. The precipitated crystals were collected by filtration, washed with cold ethanol and dried in vacuo at 40°C overnight to give 2-[2-(4-aminophenyl)ethyl]-4,5-bis(pentyloxy)-2,3-dihydroisoindol-1-one hydrochloride (17.451 g, 72%) as colorless needles.

Example 7-36

Using 3-hydroxy-5-methoxy-2-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one obtained in the same manner as in Example 7-33, 5-methoxy-2-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one was obtained as pale-yellow solid in the same manner as in Example 7-30.

Example 7-37

Using 5-methoxy-2-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one obtained in Example 7-36, 2-[2-(4-aminophenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one was obtained as colorless crystals in the same manner as in Example 7-34.

Example 7-38

2-[2-(4-Acetanilyl)ethyl]-7-methoxy-8-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one (239.4 mg, 3.88 mmol, 1.0 eq) obtained in the same manner as in Example 7-23 was dissolved in ethanol (20 ml), and 3N hydrochloric acid (20 ml) was added to this solution. The reaction mixture was refluxed under heating and

concentrated under reduced pressure. The obtained residue was purified by recrystallization from ethanol-ethyl ether to give 2-[2-(aminophenyl)ethyl]-7-methoxy-8-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one hydrochloride (165 mg, 70.0%) as colorless crystals.

Example 7-39

2-Amino-4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide (15.0 g, 37.4 mmol) obtained in Example 2-46, triethylamine (5.30 ml, 38.0 mmol) and chloroform (200 ml) were mixed, and a solution (10 ml) of triphosgene (4.75g, 16.0 mmol) in chloroform was added dropwise to this solution. After stirring at 50°C for 11.5 hours, ethanol (20 ml) was added to stop the reaction. The organic layer was washed successively with saturated aqueous sodium hydrogencarbonate solution (100 ml, 50 ml) and water (100 ml, 50 ml). This solution was dried over anhydrous magnesium sulfate, and the drying agent was filtered off. The filtrate was concentrated under reduced pressure. A hexane-chloroform solution (10:1, 110 ml) was added to the precipitated crystals, and the crystals were washed by stirring to give 7-methoxy-3-[2-(4-nitrophenyl)ethyl]-8-pentyloxy-1H-quinazoline-2,4-dione (12.56 g, 79%) as pale-yellow crystals.

Example 7-40

7-Methoxy-3-[2-(4-nitrophenyl)ethyl]-8-pentyloxy-1H-quinazoline-2,4-dione (45.0 g, 105 mmol) obtained in Example 7-39, ethanol (1300 ml) and dioxane (700 ml) were mixed, and 10% palladium-carbon catalyst (4.5 g) was added to this solution. The reaction mixture was stirred in a stream of hydrogen at room temperature for 16.5 hours, followed by filtration. Activated charcoal (2.6 g) was added to the filtrate, and the reaction mixture was stirred at 50°C for 1 hour and then filtered. The filtrate was concentrated under reduced pressure, and the obtained residue was purified by column chromatography on silica gel (chloroform/ethyl acetate = 3/1). The precipitated crude crystals were recrystallized from ethanol-hexane to give 3-[2-(4-aminophenyl)ethyl]-7-methoxy-8-pentyloxy-1H-quinazoline-2,4-dione (33.82 g, 81%) as pale-yellow crystals.

Example 7-41

3-[2-(4-Aminophenyl)ethyl]-7-methoxy-8-pentyloxy-1H-quinazoline-2,4-dione (28.0 g, 70.4 mmol) obtained in Example 7-40 and ethanol (500 ml) were

mixed, and the mixture was refluxed under heating until the crystals were completely dissolved. Concentrated hydrochloric acid (5.93 ml, 70.4 mmol) was added dropwise to this solution, and ethanol (200 ml) was further added. The mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give 3-[2-(4-aminophenyl)ethyl]-7-methoxy-8-pentyloxy-1H-quinazoline-2,4-dione hydrochloride (28.24 g, 92%) as colorless crystals.

Example 7-42

Ethyl {(4-Methoxy-2-nitro-3-pentyloxybenzoyl)-[2-(4-nitrophenyl)-ethyl]amino} acetate (70.0 mg, 0.135 mmol) and ethanol (2 ml) were mixed, and 10% palladium-carbon catalyst was added. The reaction mixture was stirred in a stream of hydrogen at room temperature for 10.5 hours, and then filtered. The filtrate was concentrated under reduced pressure. Toluene (10 ml) and p-toluene sulfonate monohydrate (1 mg, 0.0053 mmol) were added to the precipitated crude crystals, and the mixture was refluxed under heating for 3.5 hours. Ethyl acetate (20 ml) was added to this reaction mixture, and the organic layer was washed with saturated aqueous sodium hydrogencarbonate solution (5 ml) and saturated brine (5 ml) and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (chloroform/methanol = 10/1) to give 4-[2-(4-aminophenyl)ethyl]-8-methoxy-9-pentyloxy-3,4-dihydro-1H-benzo[e][1,4]diazepine-2,5-dione (35 mg, 63% in 2 steps) as colorless crystals.

Example 7-43

2-Amino-4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide (300 mg, 0.747 mmol), acetone (3 ml) and acetic acid (1.5 ml) were mixed, and the mixture was stirred at 100°C for 2 hours. Ethyl acetate (30 ml) and water (25 ml) were added to separate the organic layer. The organic layer was washed twice successively with saturated brine (20 ml), saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (20 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give a crude product of 7-methoxy-2,2-dimethyl-3-[2-(4-nitrophenyl)ethyl]-9-pentyloxy-2,3-dihydro-1H-quinazolin-4-

one.

Example 7-44

2-Amino-4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentyloxybenzamide (200 mg, 0.498 mmol) obtained in Example 2-46, ethanol (3 ml) and acetyl acetone (0.13 ml, 1.25 mmol) were mixed, and one drop of concentrated hydrochloric acid was added to this solution. The mixture was refluxed under heating for 2.5 hours, and ethyl acetate (30 ml) and saturated brine (30 ml) were added to separate the organic layer. This organic layer was washed successively with saturated aqueous sodium hydrogencarbonate solution (20 ml) and saturated brine (20 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give a crude product of 7-methoxy-2-methyl-3-[2-(4-nitrophenyl)ethyl]-8-pentyloxy-3H-quinazolin-4-one.

Example 7-45

Using 2-amino-4-methoxy-3-pentyloxy-N-(2-pyridin-4-ylethyl)benzamide (100 mg, 0.280 mmol) obtained in Example 2-61, 7-methoxy-8-pentyloxy-3-(2-pyridin-4-ylethyl)-1H-quinazoline-2,4-dione (103 mg, 96%) was obtained as colorless crystals in the same manner as in Example 7-39.

Example 7-46

2-Amino-4-methoxy-3-pentyloxy-N-(2-pyridin-4-ylethyl)benzamide (200 mg, 0.560 mmol) obtained in Example 2-61, carbon disulfide (0.6 ml), 1,8-diazabicyclo [5.4.0]-7-undecene (0.0837 ml, 0.56 mmol) and DMF (1.0 ml) were mixed, and this mixture was refluxed under heating for 4 hours. Ethyl acetate (4 ml) and water were added to this reaction mixture. The organic layer was washed with saturated aqueous sodium hydrogencarbonate solution (5 ml) and saturated brine (5 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was subjected to column chromatography on silica gel (chloroform/methanol = 10/1) and recrystallization from ethyl acetate to give 7-methoxy-8-pentyloxy-3-(2-pyridin-4-ylethyl)-2-thioxo-2,3-dihydro-1H-quinazolin-4-one (24 mg, 11%) as colorless crystals.

Example 7-47

2-Amino-4-methoxy-3-pentyloxy-N-(2-pyridin-4-ylethyl)benzamide (100 mg, 0.280 mmol) obtained in Example 2-61, dimethyl formamide dimethyl acetal (0.19 ml, 1.4 mmol) and DMF (0.5 ml) were mixed, and p-toluene sulfonate monohydrate (2 mg, 0.011 mmol) was added to this solution. The mixture was stirred at 130°C for 5 hours, and ethyl acetate (15 ml) and saturated aqueous sodium hydrogencarbonate solution (15 ml) were added to separate the organic layer. The organic layer was washed with saturated brine (15 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (chloroform/methanol = 25/1) to give 7-methoxy-8-pentyloxy-3-(2-pyridin-4-ylethyl)-3H-quinazolin-4-one (57 mg, 55%) as a pale-yellow oil.

Example 7-48

The crude product of ethyl [3-methoxy-2-pentyloxy-6-(2-pyridin-4-ylethylcarbamoyl)phenyl]acetate obtained in Example 2-51, ethanol (400 ml) and sodium ethoxide (1.98 g, 29.1 mmol) were mixed and stirred at 90°C for 30 minutes. The solvent was concentrated under reduced pressure, and 1N hydrochloric acid (100 ml), water (100 ml) and hexane-ethyl acetate solution (2:1 solution, 150 ml) were added to separate the aqueous layer. The organic layer was extracted with a mixed solution of water (100 ml) and 1N hydrochloric acid (100 ml). The aqueous layers were combined, and washed with hexane-ethyl acetate solution (2:1 solution, 150 ml). Sodium carbonate was added to the aqueous layer to make the solution alkaline under ice-cooling, and the aqueous layer was extracted twice with ethyl acetate (300 ml), and dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 1/4) to give 6-methoxy-5-pentyloxy-6-(2-pyridin-4-ylethyl)-4H-isoquinoline-1,3-dione (31.51 g, 67.5% in 2 steps) as pale-yellow crystals.

Example 7-49

6-Methoxy-5-pentyloxy-2-(2-pyridin-4-ylethyl)-4H-isoquinoline-1,3-dione (30.97 g, 80.98 mmol) obtained in Example 7-48, methylene chloride (150 ml) and

methanol (150 ml) were mixed, and sodium borohydride (6.127 g, 1623 mmol) was slowly added to this solution under ice-cooling. After stirring at room temperature for 2 hours, concentrated hydrochloric acid was added under ice-cooling to adjust the solution to pH 1, and the solution was stirred at room temperature for 30 minutes. Saturated aqueous sodium hydrogencarbonate solution was added to make the solution alkaline, and the aqueous layer was extracted with chloroform (500 ml) and the organic layer was dried over anhydrous magnesium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (ethyl acetate), and 4N hydrochloric acid-dioxane solution (40 ml) was added to the residue. Ethyl acetate (200 ml) and hexane (100 ml) were further added, and the precipitated crystals were collected by filtration. These crystals were washed twice with ethyl acetate with heating to give 6-methoxy-5-pentyloxy-2-(2-pyridin-4-ylethyl)-2H-isoquinolin-1-one hydrochloride (22.412 g, 68.7%) as colorless crystals.

Example 7-50

6-Methoxy-5-pentyloxy-1,2,3,4-tetrahydroisoquinoline (116 mg, 0.465 mmol), (4-nitrophenyl)acetate (101.1 mg, 0.558 mmol) and 1-hydroxybenzotriazol hydrate (81.7 mg, 0.605 mmol) were dissolved in DMF (2 ml), and WSC hydrochloride (125 mg, 0.651 mmol) was added to this solution under ice-cooling. After stirring at room temperature for 3 hours, ethyl acetate (3 ml) and saturated aqueous sodium hydrogencarbonate solution (3 ml) were added to the reaction mixture to separate the organic layer. The organic layer was dried over anhydrous sodium sulfate. The drying agent was filtered off and the filtrate was concentrated under reduced pressure to give a crude product of 1-(6-methoxy-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)-2-(4-nitrophenyl)ethanone. This product was used for the next reaction.

Example 7-51

The crude product of 1-(6-methoxy-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)-2-(4-nitrophenyl)ethanone obtained in Example 7-50 was dissolved in ethanol (4 ml), and 10% palladium-carbon catalyst (38 mg) was added to this solution. The reaction mixture was stirred in a stream of hydrogen for 3 hours,

and then filtered. The solvent was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 1/2) to give 2-(4-aminophenyl)-1-(6-methoxy-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)ethanone (159 mg, 89% in 2 steps) as a colorless oil.

The properties of the compounds obtained in the above Examples 7-1 to 7-51 are shown in Tables 111-127.

Examples 7-52 to 7-102

In the same manner as in the above-mentioned Example 7-1 to 7-51, the compounds shown in Example 7-52 to 7-102 were obtained. The properties of said compounds are shown in Tables 127-144.

Example 8-1

7-Methoxycoumalin (300 mg, 2.78 mmol) was dissolved in morpholine (3 ml), and the solution was refluxed under heating for 2 hours. This reaction mixture was cooled to room temperature, and water (10 ml) and saturated citric acid (50 ml) were added. The mixture was extracted twice with ethyl acetate (50 ml). The organic layers were combined, washed with saturated brine (100 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=4/1-1/2) to give (E)-[3-(6-hydroxy-4-methoxyphenyl)-1-oxo-2-propenyl]-4-morpholine (37 mg, 12.0%) as colorless crystals.

Example 8-2

(E)-[3-(6-Hydroxy-4-methoxyphenyl)-1-oxo-2-propenyl]-4-morpholine (27 mg, 0.103 mmol) was dissolved in DMF (3 ml), and to this solution were successively added 1-bromopentane (20 mg, 0.132 mmol, 1.3 eq) and anhydrous potassium carbonate (40 mg, 0.29 mmol, 2.8 eq). The mixture was stirred with heating at 90°C for 1 hour. This reaction mixture was cooled to room temperature, and water (30 ml) was added. The mixture was extracted twice with ethyl acetate (30 ml). The organic layers were combined, washed with saturated brine (30 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was

purified by column chromatography on silica gel (n-hexane/ethyl acetate=20/1) to give (E)-[3-(4-methoxy-2-pentyloxyphenyl)-1-oxo-2-propenyl]-4-morpholine (31 mg, 90.7%) as a colorless oil.

Example 8-3

4-Methoxy-3-pentyloxybenzoic acid (500 mg, 2.62 mmol, 1 eq) and 1-hydroxybenzotriazole hydrate (371 mg, 2.75 mmol, 1.05 eq) were dissolved in DMF (5 ml), and to this solution were successively added morpholine (684 mg, 7.85 mmol, 3.0 eq) and WSC hydrochloride (526 mg, 2.75 mmol, 1.05 eq) under ice-cooling. The mixture was stirred at room temperature for 12 hours. Ice water (5 ml) and a saturated aqueous sodium hydrogencarbonate solution (5 ml) were successively added to this reaction mixture. The mixture was extracted twice with ethyl acetate (20 ml). The organic layers were combined, washed with saturated brine (40 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=1/2) to give (E)-3-(3-pentyloxy-4-methoxyphenyl)-1-morpholin-4-yl-prop-2-en-1-one (343 mg, 49.8%) as a colorless solid.

Example 8-4

4-Methoxy-3-pentyloxybenzoic acid (250 mg, 1.05 mmol, 1 eq) was dissolved in thionyl chloride (1.05 ml) in a stream of nitrogen, and the solution was stirred at 70°C for 5 hours. The mixture was cooled to room temperature, and excess thionyl chloride was evaporated under reduced pressure. The residue was added to a solution of morpholine (274 mg, 3.15 mol, 3.0 eq) in DMF (3 ml) under ice-cooling. The mixture was stirred under ice-cooling for 30 minutes, and then further at room temperature for 1.5 hours. Water (30 ml) was added to this reaction mixture and the mixture was extracted twice with ethyl acetate (50 ml). The organic layers were combined, washed with saturated brine (50 ml) and dried over anhydrous sodium sulfate. The drying agent was filtered off, and the filtrate was concentrated under reduced pressure. The obtained residue was purified by column chromatography on silica gel (n-hexane/ethyl acetate=2/1) to give (4-methoxy-3-pentyloxyphenyl)morpholin-4-yl-methanone (219 mg, 67.9%) as an oil.

The properties of the compounds obtained in the above Example 8-1 to 8-4

are shown in Tables 145 and 146.

Examples 8-5 to 8-7

In the same manner as in the above Example 8-1 to 8-4, the compounds of Example 8-5 to 8-7 were obtained. The properties of obtained compounds are shown in Tables 146 and 147.

Table 1

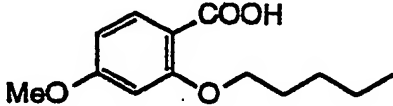
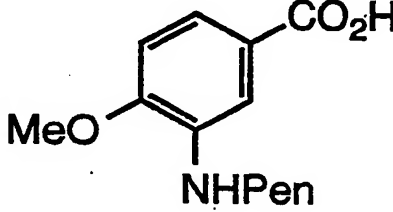
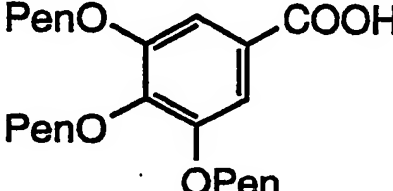
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
91	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 10.72(1H, bs), 8.14(1H, d, J = 8.8 Hz), 6.64(1H, dd, J = 8.8, 2.3 Hz), 6.51(1H, d, J = 2.3 Hz), 4.21(2H, t, J = 6.6 Hz), 3.87(3H, s), 1.83-1.95(2H, m), 1.33-1.50(4H, m), 0.95(3H, t, J = 7.0 Hz).	FAB+ 239[M+H+] (70), 221(30).
92	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.51(1H, dd, J = 8.1, 2.1 Hz), 7.29(1H, d, J = 2.1 Hz), 6.78(1H, d, J = 8.1 Hz), 3.92(3H, s), 3.18(2H, t, J = 7.2 Hz), 1.6-1.75(2H, m), 1.3-1.5(4H, m), 0.93(3H, t, J = 6.5 Hz).	
93	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.32(2H, s), 4.0-4.1(6H, m), 1.7-1.9(6H, m), 1.30-1.55(12H, m), 0.85-0.95(9H, m).	FAB+ 381[M+H+] (100), 310 (60).

Table 2

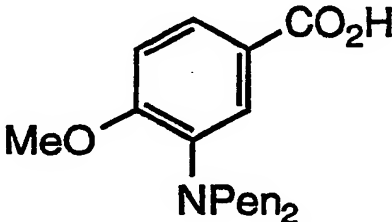
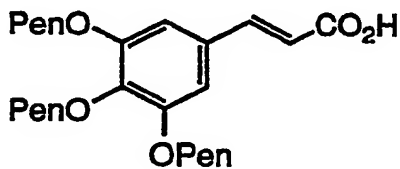
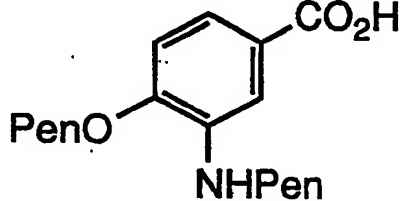
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
94	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>8.65(1H, bs), 8.22(1H, d, J = 9.0 Hz), 7.14(1H, d, J = 9.0 Hz), 4.06(3H, s), 3.54(4H, bt), 1.8-2.1(1H, m), 1.0-1.4(11H, m), 0.81(6H, bt).</p>	<p>FAB+</p> <p>308[M+H+] (100), 250(30).</p>
95	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.67(1H, d, J = 16 Hz), 7.75(2H, s), 6.31(1H, d, J = 16 Hz), 3.9-4.1(6H, m), 1.7-1.9(6H, m), 1.30-1.55(12H, m), 0.87-1.0(9H, m).</p>	<p>FAB+</p> <p>407[M+H+] (90), 336(60).</p>
96	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.47(1H, dd, J = 8.4, 2.1 Hz), 7.28(1H, d, J = 2.0 Hz), 6.76(1H, d, J = 8.4 Hz), 4.06(2H, t, J = 6.6 Hz), 3.18(2H, t, J = 7.1 Hz), 1.78-1.92(2H, m), 1.62-1.74(2H, m), 1.30-1.53(8H, m), 0.94(3H, t, J = 7.0 Hz), 0.93(3H, t, J = 7.0 Hz).</p>	<p>FAB+</p> <p>294[M+H+] (50), 277(60), 185(100).</p>

Table 3


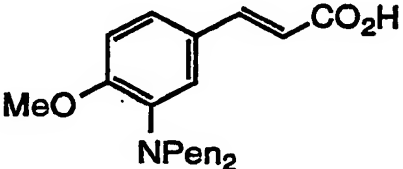
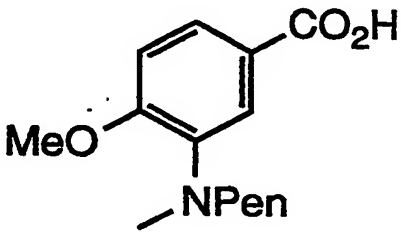
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
97	 <p>Yellow crystals</p>	CDCl ₃ ,300MHz 7.71(1H, d, J=16 Hz), 6.86(1H, dd, J=8.2,2.0Hz), 6.77(1H, s), 6.74(1H, d, J=8.2 Hz), 6.29(1H, d, J=16 Hz), 3.88(3H, s), 3.14(2H, t, J=7.1 Hz), 1.6-1.75(2H, m), 1.3-1.5(4H, m), 0.94(3H, t, J=7.0 Hz).	FAB+ 264[M+H+] (50), 237(100), 206(40).
98	 <p>Yellow crystals</p>	CDCl ₃ ,300MHz 7.72(1H, d, J=16 Hz), 7.18(1H, dd, J=8.4,2.0Hz), 7.12(1H, d, J=2.0 Hz), 6.85(1H, d, J=8.4 Hz), 6.30(1H, d, J=16 Hz), 3.88(3H, s), 3.08(4H, t, J=7.7 Hz), 1.37-1.54(4H, m), 0.25-1.36(8H, m), 0.87(6H, t, J=6.9 Hz).	FAB+ 334[M+H+] (100), 276(30).
99	 <p>Pale-yellow oil</p>	CDCl ₃ ,300MHz 7.77(1H, dd, J=8.5,2.1Hz), 7.66(1H, d, J=2.0 Hz), 6.88(1H, d, J=8.5 Hz), 3.94(3H, s), 3.04(2H, t, J=7.8 Hz), 2.82(3H, s), 1.45-1.60(2H, m), 1.2-1.4(4H, m), 0.89(3H, t, J=6.9 Hz).	FAB+ 252[M+H+] (100), 194(50).

Table 4

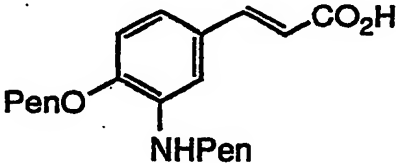
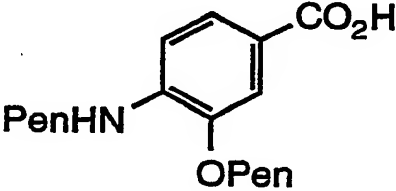
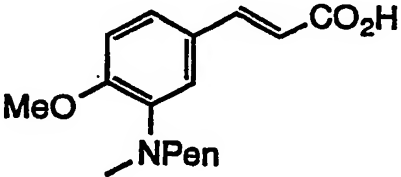
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
100	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.72(1H, d, J=16 Hz), 6.84(1H, dd, J=8.1, 1.8 Hz), 6.77(1H, d, J=2.4 Hz), 6.72(1H, d, J=8.1 Hz), 6.30(1H, d, J=16 Hz), 4.03(2H, t, J=6.3 Hz), 3.15(2H, t, J=7.1 Hz), 1.75-1.90(2H, m), 1.60-1.73(2H, m), 1.30-1.50(8H, m), 0.94(6H, t, J=6.9 Hz).</p>	<p>FAB+</p> <p>320[M+H+] (70), 262(20).</p>
101	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.69(1H, dd, J=8.1, 1.5 Hz), 7.41(1H, d, J=1.8 Hz), 6.54(1H, d, J=8.1 Hz), 4.05(2H, t, J=6.5 Hz), 3.20(2H, t, J=7.1 Hz), 1.75-1.90(2H, m), 1.60-1.75(2H, m), 1.30-1.50(8H, m), 0.85-1.2(6H, m).</p>	<p>FAB+</p> <p>294[M+H+] (50), 293(100), 236(20).</p>
102	 <p>Pale-yellow crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.72(1H, d, J=16 Hz), 7.17(1H, bs), 6.88(1H, bs), 6.33(1H, s, J=16 Hz), 3.92(3H, s), 3.07(2H, bs), 2.82(3H, bs), 1.4-1.6(2H, m), 1.2-1.4(4H, m), 0.88(3H, t, J=6.8 Hz).</p>	<p>FAB+</p> <p>278[M+H+] (100), 220(30).</p>

Table 5

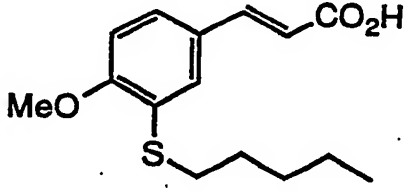
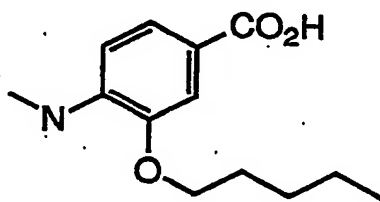
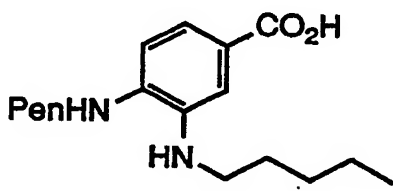
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
103	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.72(1H, d, J = 16 Hz), 7.42(1H, d, J = 2.1 Hz), 7.36(1H, dd, J = 8.5, 2.1 Hz), 6.85(1H, d, J = 8.5 Hz), 6.33(1H, d, J = 16 Hz), 3.93(3H, s), 2.91(2H, t, J = 7.4 Hz), 1.60-1.75(2H, m), 1.30-1.50(4H, m), 0.91(3H, t, J = 7.1 Hz).</p>	<p>FAB+</p> <p>281[M+H+] (60), 280(100).</p>
104	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.73(1H, d, J = 8.4 Hz), 7.43(1H, s), 6.54(1H, d, J = 8.4 Hz), 4.05(2H, t, J = 6.3 Hz), 2.94(3H, s), 1.73-1.90(2H, m), 1.30-1.55(4H, m), 0.94(3H, t, J = 6.9 Hz).</p>	<p>FAB+</p> <p>238[M+H+] (80), 220(60), 169(100).</p>
105	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>7.67(1H, dd, J = 8.4, 1.8 Hz), 7.41(1H, d, J = 1.8 Hz), 6.61(1H, d, J = 8.4 Hz), 3.18(2H, t, J = 8.3 Hz), 3.12(2H, t, J = 8.3 Hz), 1.6-1.8(4H, m), 1.30-1.50(8H, m), 0.94(6H, t, J = 6.9 Hz).</p>	<p>293[M+H+] (40), 292(100).</p>

Table 6

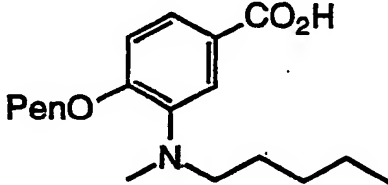
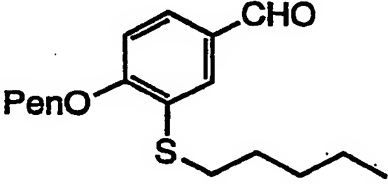
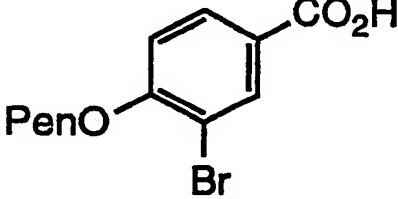
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
106	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.71(1H, dd, J=8.4, 2.1 Hz), 7.62(1H, d, J=2.1 Hz), 6.86(1H, d, J=8.4 Hz), 4.06(2H, t, J=6.6 Hz), 3.05(2H, t, J=7.7 Hz), 2.83(3H, s), 1.80-1.95(2H, m), 1.20-1.65(10H, m), 0.94(6H, t, J=7.0 Hz), 0.89(6H, t, J=7.0 Hz).	FAB+ 308[M+H+] (20), 185(100).
107	 <p>Pale-yellow oil</p>	CDCl ₃ , 300MHz 9.85(1H, s), 7.72(1H, d, J=2.1 Hz), 7.63(1H, dd, J=8.4, 1.8 Hz), 6.91(1H, d, J=8.4 Hz), 2.94(2H, t, J=7.4 Hz), 1.80-1.93(2H, m), 1.6-1.78(2H, m), 1.20-1.60(8H, m), 0.94(3H, t, J=7.2 Hz), 0.92(3H, t, J=7.2 Hz).	FAB+ 295[M+H+] (80), 294(100), 225(40).
108	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 8.29(1H, d, J=2.1 Hz), 8.02(1H, dd, J=9.0, 2.4 Hz), 6.91(1H, d, J=9.0 Hz), 4.10(2H, t, J=6.5 Hz), 1.80-1.95(2H, m), 1.30-1.60(4H, m), 0.95(3H, t, J=7.2 Hz).	FAB+ 288[M+H+] (30), 218(30).

Table 7

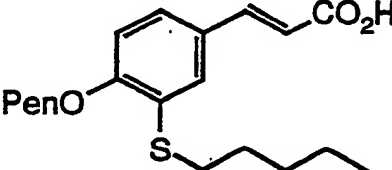
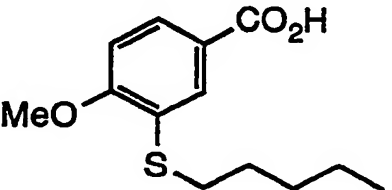
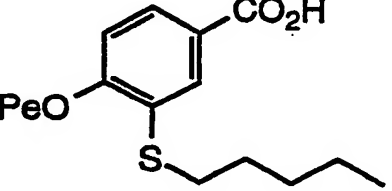
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
109	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.71(1H, d, J=16 Hz), 7.41(1H, d, J=2.4 Hz), 7.33(1H, dd, J=8.7, 1.8 Hz), 6.83(1H, d, J=8.7 Hz), 6.31(1H, d, J=16 Hz), 4.06(2H, t, J=6.5 Hz), 2.90(2H, t, J=7.4 Hz), 1.80-1.95(2H, m), 1.60-1.77(2H, m), 1.30-1.56(8H, m), 0.94(3H, t, J=8.0 Hz), 0.91(3H, t, J=8.0 Hz).	FAB+ 337[M+H+] (50), 266(50).
111	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.95(1H, s), 7.93(1H, d, J=8.4 Hz), 6.88(1H, d, J=8.4 Hz), 3.97(3H, s), 2.95(2H, t, J=7.4 Hz), 1.65-1.80(2H, m), 1.30-1.55(4H, m), 0.91(3H, t, J=7.2 Hz).	FAB+ 255[M+H+] (30), 254(40).
112	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.94(1H, d, J=2.0 Hz), 7.89(1H, dd, J=8.5, 2.0 Hz), 6.85(1H, d, J=2.0 Hz), 4.10(2H, t, J=6.6 Hz), 2.94(2H, t, J=7.4 Hz), 1.77-1.95(2H, m), 1.60-1.75(2H, m), 1.3-1.5(8H, m), 0.91(3H, t, J=7.1 Hz).	FAB+ 311[M+H+] (50), 310(100), 240(40).

Table 8

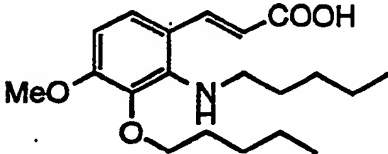
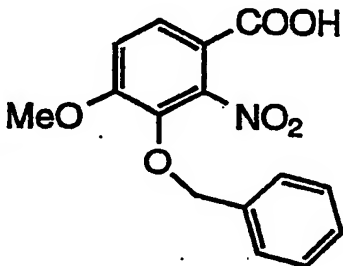
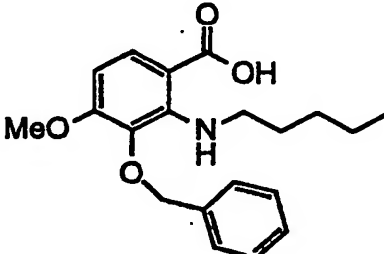
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
113	 <p>Colorless crystals</p>		
114	 <p>Colorless crystals</p>		
115	 <p>Colorless crystals</p>		

Table 9

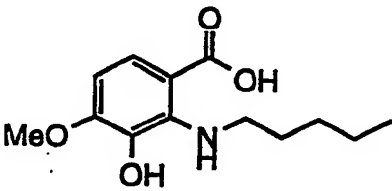
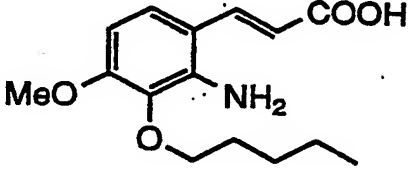
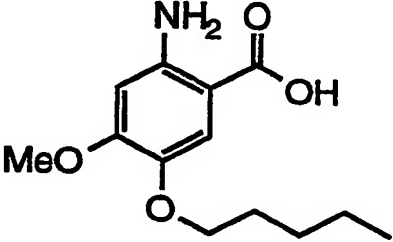
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
116	 <p>Brown crystals</p>	DMSO-d ₆ , 300MHz 7.39(1H, d, J=8.8Hz) 6.48(1H, d, J=8.8Hz) 3.80(3H, s) 3.32(2H, t, J=6.9Hz) 1.35-1.50(2H, m) 1.20-1.33(4H, m) 0.85(3H, t, J=7.0Hz)	
117	 <p>Pale-yellow crystals</p>	CDCl ₃ , 300MHz 7.87(1H, d, J=15.6Hz) 7.17(1H, d, J=8.7Hz) 6.39(1H, d, J=8.7Hz) 6.27(1H, d, J=15.6Hz) 3.96(2H, t, J=6.8Hz) 3.86(3H, s) 1.70-1.85(2H, m) 1.30-1.50(4H, m) 0.94(3H, t, J=7.1Hz)	
118	 <p>Gray crystals</p>	CDCl ₃ , 300MHz 7.37(1H, s) 6.13(1H, s) 3.94(2H, t, J=6.8Hz) 3.86(3H, s) 1.75-1.85(2H, m) 1.35-1.50(4H, m) 0.93(3H, t, J=7.2Hz)	

Table 10

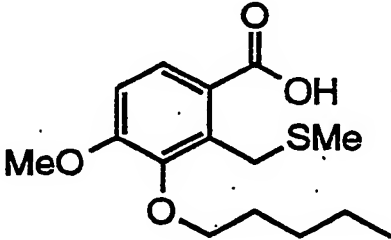
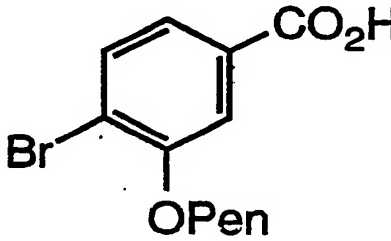
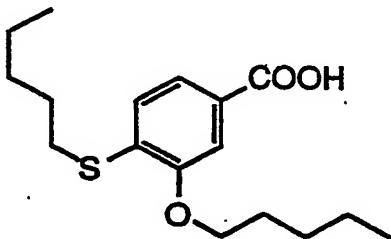
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
119	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.86(1H, d, J=8.8Hz) 6.84(1H, d, J=8.8Hz) 4.26(2H, s) 3.97(2H, t, J=6.7Hz) 3.91(3H, s) 2.09(3H, s) 1.75-1.90(2H, m) 1.30-1.50(4H, m) 0.95(3H, t, J=7.1Hz)	FAB+ 299[M+H+] (50) 289(60)
120	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 8.29(1H, d, J = 2.1 Hz) 8.02(1H, dd, J = 9.0, 2.4 Hz) 6.91(1H, d, J = 9.0 Hz) 4.10(2H, t, J = 6.5 Hz) 1.80-1.95(2H, m) 1.30-1.60(4H, m) 0.95(3H, t, J = 7.2 Hz)	288[M+H+] (30) 218(30)
121	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.66(1H, d, J=9.0Hz) 7.47(1H, s) 7.19(1H, d, J=9.0Hz) 4.09(2H, t, J=6.6Hz) 2.93(2H, t, J=7.4Hz) 1.30-1.90(12H, m) 0.94(3H, t, J=7.5Hz) 0.92(3H, t, J=7.5Hz)	FAB+ 311[M+H+] (50) 310(100) 240(40)

Table 11

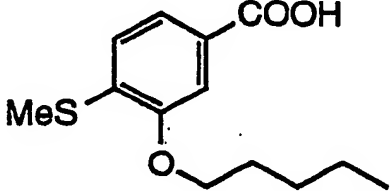
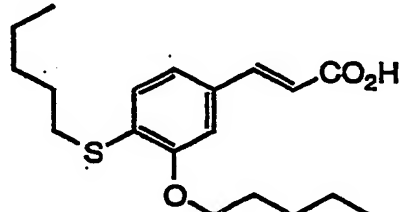
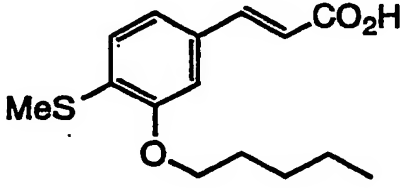
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
122	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.71(1H, d, J=8.2Hz) 7.48(1H, s) 7.14(1H, d, J=8.2Hz) 4.11(2H, t, J=6.5Hz) 2.47(3H, s) 1.80-1.90(2H, m) 1.30-1.55(4H, m) 0.95(3H, t, J=7.2Hz)	FAB+ 255[M+H] (30) 254(50)
123	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.71(1H, d, J=16.2Hz) 7.08-7.19(2H, m) 6.97(1H, s) 6.38(1H, d, J=16.2Hz) 4.06(2H, t, J=6.5Hz) 2.912(2H, t, J=7.5Hz) 1.30-1.95(12H, m) 0.87-0.98(6H, m)	FAB+ 337[M+H] (40) 336(100)
124	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.72(1H, d, J=15.9Hz) 7.08-7.15(2H, m) 6.96(1H, s) 6.39(1H, d, J=15.9Hz) 4.06(2H, t, J=6.5Hz) 2.45(3H, s) 1.80-1.90(2H, m) 1.35-1.60(4H, m) 0.95(3H, t, J=7.4Hz)	FAB+ 281[M+H] (20) 280(40)

Table 12

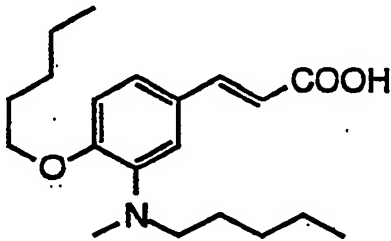
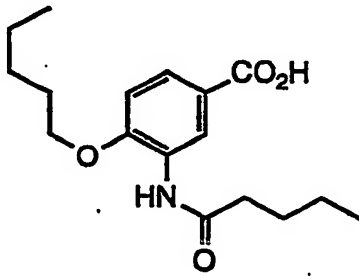
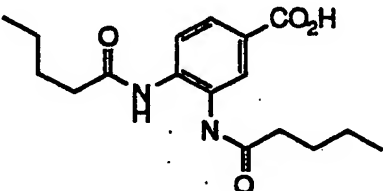
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
125	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 7.72(1H, d, J=15.9Hz) 7.11(1H, d, J=8.2Hz) 7.10(1H, s) 6.82(1H, d, J=8.2Hz) 6.30(1H, d, J=15.9Hz) 4.05(2H, t, J=6.6Hz) 3.05(2H, t, J=7.8Hz) 2.81(3H, s) 1.80-1.95(2H, m) 1.20-1.65(10H, m) 0.94(3H, t, J=7.1Hz) 0.89(3H, t, J=7.1Hz)	
126	 <p>Colorless crystals</p>	CDCl ₃ , 300MHz 9.04(1H, bs) 7.82(1H, d, J=8.7Hz) 7.72(1H, bs) 6.90(1H, d, J=8.7Hz) 4.11(2H, t, J=6.6Hz) 2.42(2H, t, J=7.5Hz) 1.63-1.94(4H, m) 1.33-1.53(6H, m) 0.96(6H, t, J=7.4Hz)	
127	 <p>Colorless crystals</p>		FAB+ 321[M+H] ⁺ (60) 219(100)

Table 13

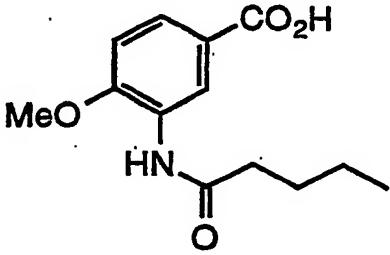
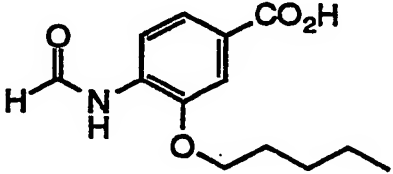
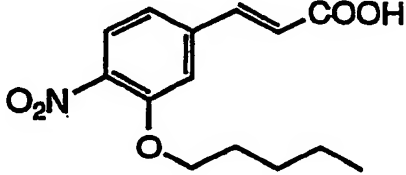
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
128	 <p>Colorless crystals</p>	<p>CDCl₃, 300MHz</p> <p>9.05(1H,bs) 7.83(1H,d,J=8.7Hz) 6.91(1H,d,J=8.7Hz) 3.95(3H,s) 2.41(2H,t,J=7.5Hz) 1.65-1.80(2H,m) 1.35-1.48(2H,m) 0.95(3H,t,J=7.3Hz)</p>	<p>FAB+</p> <p>252[M+H+] (70) 185(100)</p>
129	 <p>Colorless crystals</p>	<p>DMSO-d₆, 300MHz</p> <p>12.8(1H,s) 9.71(1H,s) 8.40(1H,s) 8.32(1H,d,J=8.4Hz) 7.52(1H,d,J=8.4Hz) 7.59(1H,s) 4.07(2H,t,J=6.6Hz) 1.75-1.83(2H,m) 1.30-1.50(4H,m) 0.90(3H,t,J=7.1Hz)</p>	<p>FAB+</p> <p>252[M+H+] (100) 182(100)</p>
130	 <p>Pale-yellow crystals</p>		

Table 14

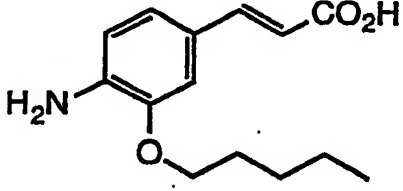
Prep. Ex.	Structural formula	¹ H NMR (δ) ppm	MS
131	 <p>Pale-yellow crystals</p>	DMSO-d ₆ , 300MHz 7.26(1H, d, J=15.7Hz) 7.03(1H, s) 6.89(1H, d, J=8.2Hz) 6.59(1H, d, J=8.2Hz) 6.19(1H, d, J=15.7Hz) 5.08(2H, bs) 3.98(2H, t, J=6.5Hz) 1.68-1.80(2H, m) 1.27-1.50(4H, m) 0.90(3H, t, J=7.1Hz)	FAB+ 250[M+H] (60) 249(100)

Table 15

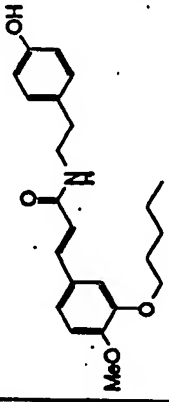
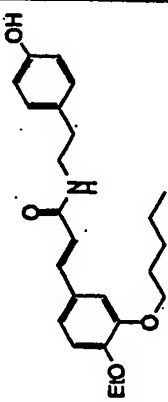
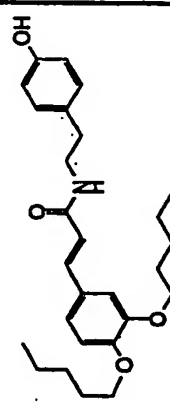
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
1-1		106.5~ 107.3°C	CDCl ₃ -300MHz 7.54(1H, d, J=15.5, 15.3 Hz) 2.80(2H, t, J=6.8 Hz) 7.05(2H, d, J=8.4 Hz) 1.7-1.9(2H, m) 7.05(1H, dd, J=8.2, 1.9 Hz) 1.3-1.5(4H, m) 7.00(1H, d, J=1.9 Hz) 0.93(3H, t, J=7.0 Hz) 6.83(1H, d, J=8.2 Hz) 6.81(2H, d, J=8.4 Hz) 6.18(1H, d, J=15.5 Hz) 6.09(1H, bs) 5.6-5.7(1H, m) 4.00(2H, t, J=6.8 Hz) 3.87(3H, s) 3.61(2H, q, J=6.8 Hz)	KBr 3231 1646 1516	FAB+ 384 [M ⁺ H] ⁺ (50) 136(100)	C ₁₀ H ₁₁ N ₁₂ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 72.04% H: 7.81% N: 3.64%
1-2		126~ 127°C	(DMSO-d ₆ , 300MHz) 9.14(1H, s) 7.97(1H, t) 7.31(1H, d, J=15.8 Hz) 6.93-7.12(5H, m) 6.67(2H, d, J=8.4 Hz) 6.46(1H, d, J=15.8 Hz) 4.04(2H, t, J=6.9 Hz) 3.97(2H, t, J=6.6 Hz) 3.26-3.37(2H, m) 2.63(2H, t, J=6.5 Hz) 1.66-1.77(2H, m) 1.26-1.46(7H, m)	0.89(3H, t, J=7.2 Hz)	FAB+ 398 [M ⁺ H] ⁺ (52) 276(23) 261(100) 190(85) 162(86)	
1-3		126~ 127°C	(DMSO-d ₆ , 300MHz) 9.15(1H, s) 7.97(1H, t) 7.32(1H, d, J=15.7 Hz) 6.94-7.13(5H, m) 6.68(2H, d, J=8.4 Hz) 6.47(1H, d, J=15.7 Hz) 3.95-4.00(4H, m) 3.25-3.38(2H, m) 2.65(2H, t, J=7.5 Hz) 1.64-1.78 (4H, m) 1.27-1.47(8H, m) 0.81-0.94(6H, m)		FAB+ 440 [M ⁺ H] ⁺ (50) 318(14) 303(44) 232(32) 162(100)	

Table 16

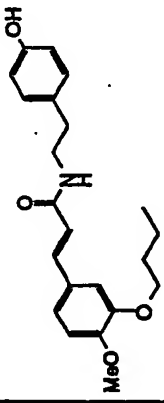
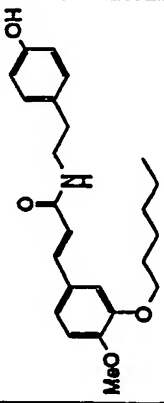
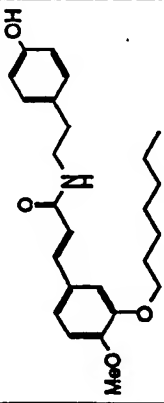
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm} ⁻¹	MS	Elen. anal.
1-4	 <p>Colorless crystals</p>	123~ 125°C	(DMSO-d ₆ , 300MHz) 9.15(1H, s) 7.98(1H, t, J=5.5 Hz) 7.33(1H, d, J=15.7 Hz) 7.13(1H, d, J=2.0 Hz) 7.09(1H, dd, 8.4, 2.0 Hz) 7.01(2H, d, J=8.4 Hz) 6.97(1H, d, J=8.3 Hz) 6.68(2H, d, J=8.4 Hz) 6.48(1H, d, J=15.8 Hz) 3.98(2H, d, J=6.5 Hz) 3.78(3H, s) 3.78(3H, s)	KBr 3484 3305 1644 1589 1549 1516 1260 1241 1140 1018	FAB+ 370 [M ⁺ H] ⁺ (100) 248(31) 233(58) 176(76)	
1-5	 <p>Colorless crystals</p>	117~ 118°C	(DMSO-d ₆ , 300MHz) 9.14(1H, s) 7.97(1H, t, J=5.6 Hz) 7.32(1H, d, J=15.7 Hz) 7.12(1H, d, J=2.0 Hz) 7.09(1H, dd, 8.3, 2.0 Hz) 7.01(2H, d, J=8.4 Hz) 6.96(1H, d, J=8.3 Hz) 6.68(2H, d, J=8.3 Hz) 6.47(1H, d, J=15.8 Hz) 3.97(2H, t, J=6.6 Hz) 3.78(3H, s) 3.33(2H, m)	KBr 3436 2952 1652 1614 1594 1548 1514 1342 1259 1243	FAB+ 398 [M ⁺ H] ⁺ (33) 397[M] ⁺ (32) 276(25) 261(36) 176(69) 153(100)	
1-6	 <p>Colorless crystals</p>	123~ 124°C	(DMSO-d ₆ , 300MHz) 9.14(1H, s) 7.97(1H, t, J=5.6 Hz) 7.32(1H, d, J=15.9 Hz) 7.12(1H, d, J=2.0 Hz) 7.08(1H, dd, 8.3, 2.0 Hz) 7.00(2H, d, J=8.4 Hz) 6.95(1H, d, J=8.3 Hz) 6.68(2H, d, J=8.3 Hz) 6.47(1H, d, J=15.8 Hz) 3.96(2H, t, J=6.6 Hz) 3.78(3H, s) 3.33(2H, m)	KBr 3280 2933 1630 1614 1598 1538 1516 1259 1237 1138	FAB+ 412 [M ⁺ H] ⁺ (66) 290(22) 275(28) 176(52) 168(100)	C ₂₃ H ₂₇ NO ₄ Calcd. C: 72.96% H: 8.08% N: 3.40% Found C: 72.96% H: 8.23% N: 3.37%

Table 17

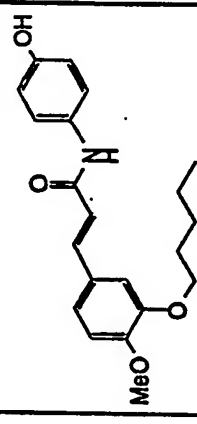
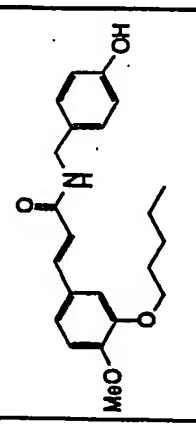
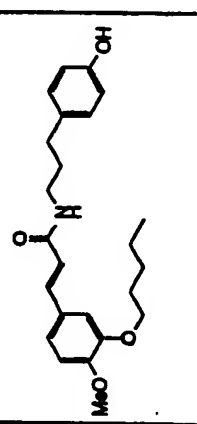
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-7		176.6~ 177.2°C	(DMSO-d ₆ , 300MHz) 9.8(1H, s) 9.2(1H, s) 7.5(2H, d, J=9 Hz) 7.4(1H, d, J=18 Hz) 7.2(1H, s) 7.1(1H, d, J=6 Hz) 7.0(1H, d, J=6 Hz) 6.7(2H, d, J=9 Hz) 6.6(1H, d, J=18 Hz) 4.0(2H, t, J=7.5 Hz) 3.8(3H, s) 1.7-1.8(2H, m)	KBr 3280 2934 1654 1619 1511	FAB+ 356 [M ⁺ H] ⁺ (20) 169(100)	C ₂₁ H ₂₃ NO ₄ Calcd. C: 70.96% H: 7.09% N: 3.94% Found C: 70.66% H: 7.23% N: 4.08%
1-8			(CDCl ₃ , 300MHz) 7.6(1H, d, J=15 Hz) 7.1(2H, d, J=9 Hz) 7.0(1H, d, J=9 Hz) 7.0(1H, s) 6.8(2H, d, J=9 Hz) 6.6(1H, bs) 6.3(1H, d, J=15 Hz) 6.0(1H, bs) 4.5(2H, d, J=3 Hz) 4.0(2H, t, J=7.5 Hz) 3.9(3H, s) 1.8-1.9(2H, m)	KBr 3221 1513 1264	FAB+ 370 [M ⁺ H] ⁺ (40)	C ₂₁ H ₂₃ NO ₄ Calcd. C: 71.52% H: 7.37% N: 3.79% Found C: 71.64% H: 7.48% N: 3.82%
1-9			CDCl ₃ , 300MHz 7.51(1H, d, J=15.5 Hz) 7.04(1H, dd, J=8.4, 2.4 Hz) 7.00(1H, d, J=2.4 Hz) 7.00(2H, d, J=8.3 Hz) 6.82(1H, d, J=8.4 Hz) 6.76(2H, d, J=8.3 Hz) 6.51(1H, bs) 6.21(1H, d, J=15.5 Hz) 5.73(1H, bs) 4.00(2H, t, J=6.8 Hz) 3.86(3H, s) 3.38(2H, q, J=6.7 Hz)	Neat 3300 2932 1652 1594 1514 1260	FAB+ 398 [M ⁺ H] ⁺ (95) 247(50) 177(100)	

Table 18

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-10			CDCl ₃ , 300MHz 7.52(1H, d, J=15.5 Hz) 7.27(1H, bs) 7.16(1H, t, J=7.6 Hz) 7.01(1H, dd, J=8.3, 1.8 Hz) 6.97(1H, d, J=1.8 Hz) 6.80(1H, d, J=8.3 Hz) 6.77(1H, d, J=7.6 Hz) 6.76(1H, s) 6.71(1H, t, J=7.6 Hz) 6.19(1H, d, J=15.5 Hz) 5.82(1H, bs) 3.97(2H, t, J=6.8 Hz)	Neat 3280 2933 1656 1586 1573 1260	FAB+ [M ⁺ H] ⁺ (40) HRFAB(m/z) Calcd. C ₂₃ H ₂₆ NO ₄ 384.5006 Found 384.2166	C ₂₃ H ₂₆ NO ₄
1-11			CDCl ₃ , 300MHz 7.82(1H, bs) 7.60(1H, d, J=15.5 Hz) 7.14(1H, t, J=7.9 Hz) 7.06(1H, d, J=8.5 Hz) 7.06(1H, d, J=7.9 Hz) 7.01(1H, s) 6.92(1H, d, J=7.9 Hz) 6.83(1H, d, J=8.5 Hz) 6.81(1H, d, J=7.9 Hz) 6.24(1H, d, J=15.5 Hz) 6.17(1H, bs) 4.01(2H, t, J=6.8 Hz)	Neat 3280 1655 1594 1513 1260	FAB+ 384 [M ⁺ H] ⁺ (100)	
1-12			CDCl ₃ , 300MHz 7.54(1H, d, J=15.5 Hz) 7.07(1H, dd, J=8.3, 1.9 Hz) 7.02(1H, d, J=1.9 Hz) 6.85(1H, d, J=8.3 Hz) 6.23(1H, d, J=15.5 Hz) 5.52(1H, bs) 4.02(2H, t, J=6.9 Hz) 3.88(3H, s) 3.9-4.1(0.5H, m) 3.5-3.7(0.5H, m) 3.3-3.5(2H, m) 1.9-2.1(2H, m)	Neat 3288 2927 1513 1260	FAB+ [M ⁺ H] ⁺ (40) 247(35) HRFAB(m/z) Calcd. C ₂₃ H ₂₆ NO ₄ 390.5486 Found 390.2638	

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-13	<p>Colorless crystals</p>	125~ 126°C	CDCl ₃ , 300MHz 8.53-8.55(2H, m) 7.56 (1H, d, J=15.7 Hz) 7.16-7.18(2H, m) 7.06(1H, dd, J=8.0, 2.1 Hz) 7.01(1H, d, J=2.1 Hz) 6.85(1H, d, J=8.0 Hz) 6.19(1H, d, J=15.7 Hz) 5.01 (1H, t) 4.06(2H, t, J=7.2 Hz) 3.88(3H, s) 3.68 (2H, q, J=6.9 Hz) 2.91(2H, t, J=6.9 Hz)	Neat 3301 2949 1615 1263	FAB+ 369 [M ⁺ H] ⁺ (100)	C ₂₂ H ₂₀ N ₂ O ₃ Calcd. C: 71.71% H: 7.66 % N: 7.60 % Found C: 71.63% H: 7.82% N: 7.59 %
1-14	<p>Colorless crystals</p>	91~ 93°C	CDCl ₃ , 300MHz 8.53-8.60(1H, m) 7.63(1H, td, J=7.7, 1.8 Hz) 7.53(1H, d, J=15.6 Hz) 7.03-7.22(4H, m) 6.84 (1H, d, J=8.3 Hz) 6.63(1H, br s) 6.25(1H, d, J= 15.6 Hz) 4.03(2H, t, J=6.9 Hz) 3.88(3H, s) 3.81(2H, q, J=6.2 Hz) 3.07(2H, t, J=6.2 Hz) 1.81-1.89(2H, m)	Neat 3249 2951 1654 1592 1513 1258 1134	FAB+ 369 [M ⁺ H] ⁺ (100) 289(23) 247(59) 177(72)	C ₂₂ H ₂₀ N ₂ O ₃ Calcd. C: 71.71% H: 7.66 % N: 7.60 % Found C: 71.76% H: 7.85% N: 7.56 %
1-15	<p>Pale-yellow oil</p>		CDCl ₃ , 300MHz 8.43-8.59(2H, m) 7.50-7.64(2H, m) 7.50(1H, d, J=15.3 Hz) 7.02-7.16(5H, m) 7.01(1H, d, J= 1.9 Hz) 6.84(1H, d, J=8.3 Hz) 6.61(1H, d, J= 15.3 Hz) 4.05(2H, t, J=6.8 Hz) 3.89(3H, s) 3.73-3.86(4H, m) 2.98-3.20(4H, m) 1.77-1.95(2H, m)	Neat 1645 1592 1434 1261 1139	FAB+ 474 [M ⁺ H] ⁺ (100) 247(81) 177(99)	

Table 20

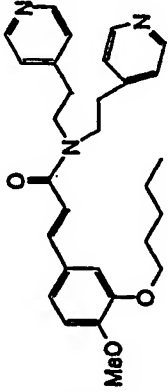
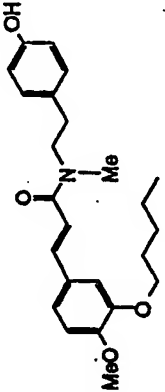
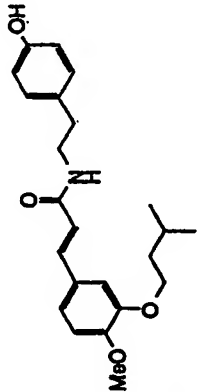
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ¹	MS	Elem. anal.
1-16	 <p>Colorless crystals</p>	114~ 116°C	CDCl ₃ , 300MHz 8.52-8.54(4H, m) 7.61(1H, d, J=15.0 Hz) 7.05-7.20(4H, m) 7.05(1H, dd, J=8.8, 1.9 Hz) 6.95(1H, d, J=1.9 Hz) 6.87(1H, d, J=8.8 Hz) 6.47(1H, d, J=1.5 Hz) 4.03(2H, t, J=6.7 Hz) 3.90 (3H, s) 3.50-3.67(4H, m) 2.80-2.99(4H, m) 1.83-1.94(2H, m)	Neat 2953 1642 1596 1510 1260	FAB+ 474 [M ⁺ H] ⁺ (36) 369(23) 247(50) 177(73) 106(100)	C ₂₂ H ₂₃ N ₂ O ₂ Calcd. C: 73.54% H: 7.45 % N: 8.87% Found C: 73.65% H: 7.62% N: 8.88 %
1-17			CDCl ₃ , 300MHz 7.44(1H, d, J=15.4 Hz) 7.00(2H, d, J=8.3 Hz) 6.77-7.1(4H, m) 6.77(2H, d, J=8.3 Hz) 6.31(1H, d, J=15.4 Hz) 4.02(2H, t, J=6.7 Hz) 3.87(3H, s) 3.63-3.7(2H, m) 2.99(3H, s) **2.8-2.9(2H, J) 1.8-1.9(2H, m) 1.3-1.5(4H, m)	Neat 3220 2931 1643 1584 1514	FAB+ 398 [M ⁺ H] ⁺ (70) 247(100) 177(80)	
1-18	 <p>Colorless crystals</p>	91~ 92°C	DMSO-d6, 300MHz 9.14(1H, s) 7.98(1H, t) 7.32(1H, d, 15.8 Hz) 6.94-7.15(5H, m) 6.67(2H, d, J=8.4 Hz) 6.47(1H, d, J=15.8 Hz) 3.99(2H, t, J=6.7 Hz) 3.77(3H, s) 3.29-3.36(2H, m) 2.64(2H, t, J=7.5 Hz) 1.70-1.85(1H, m) 1.61(2H, q, J=6.7 Hz)		FAB+ 384 [M ⁺ H] ⁺ (70) 247(44) 176(100)	

Table 21

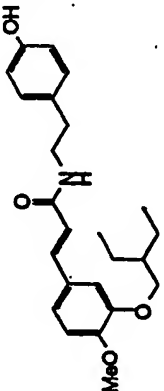
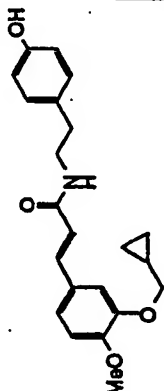
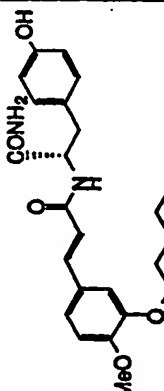
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-19	 <p>Pale-yellow oil</p>		DMSO-d ₆ , 300MHz 9.15(1H, s) 7.98(1H, t) 7.31(1H, d, J=15.8 Hz) 6.94-7.15(5H, m) 6.68(2H, d, J=8.4 Hz) 6.47(1H, d, J=15.8 Hz) 3.86(2H, d, J=5.8 Hz) 3.78(3H, s) 3.27-3.39(2H, m) 2.64(2H, t, J=7.2 Hz) 1.57-1.68(1H, m) 1.33-1.53(4H, m)		FAB+ 398 [M ⁺ H] ⁺ (24) 261(14) 176(100)	
1-20	 <p>Colorless crystals</p>	135~ 136°C	DMSO-d ₆ , 300MHz 9.14(1H, s) 7.97(1H, t, J=5.7 Hz) 7.30(1H, d, J=15.6 Hz) 6.94-7.09(5H, m) 6.67(2H, d, J=8.4 Hz) 6.46(1H, d, J=15.6 Hz) 3.81(2H, d, J=6.9 Hz) 3.78(3H, s) 3.29-3.35(2H, m) 2.63(2H, t, J=7.5 Hz) 1.14-1.29(1H, m) 0.53-0.60(2H, m)		FAB+ 368 [M ⁺ H] ⁺ (37) 231(36) 176(100)	
1-21			CDCl ₃ , 300MHz 7.56(1H, d, J=15.6 Hz) 7.17(2H, d, J=8.51 Hz) 7.07(1H, d, J=8.27 Hz) 7.03(1H, s) 6.85(1H, d, J=8.27 Hz) 6.79(2H, d, J=8.51 Hz) 6.25(1H, d, J=15.6 Hz) 6.17(1H, d, J=7.58 Hz) 5.68(1H, br) 5.28(1H, br) 4.70-4.80(2H, m) 4.03(2H, t, J=6.89 Hz)	KBr 3600- 3000 1652 1612	FAB+ 427 [M ⁺ H] ⁺ (20) 247(50) 136(70)	C ₂₄ H ₂₉ N ₃ O ₃ Calcd. C: 67.59% H: 7.09% N: 6.57% Found C: 67.30% H: 7.17% N: 6.55 %

Table 22

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-22			CDCl ₃ , 300MHz 7.55(1H, d, J=15.6 Hz) 7.04(1H, d, J=8.3 Hz) 7.01(1H, s) 6.96(2H, d, J=8.4 Hz) 6.83(1H, d, J=8.3 Hz) 6.73(2H, d, J=8.4 Hz) 6.26(1H, d, J=15.6 Hz) 6.20(1H, bs) 6.13(1H, bd) 4.9-5.1(1H, m) 4.01(2H, t, J=6.8 Hz) 3.88(3H, s)	Neat 3283 1747 1658 1514 1261	442 [M ⁺ H] ⁺ (60) 247(100) HRFAB(m/z) Calcd. C ₂₃ H ₂₃ NO ₆ 442.5370 Found 442.2238	
1-23		188~ 190°C	DMSO-d ₆ , 300MHz 8.55(2H, s) 7.95(1H, d, J=8.0 Hz) 7.34(1H, d, J=16.0 Hz) 7.14(1H, d, J=2.0 Hz) 7.09(1H, dd, 8.2, 2.0 Hz) 6.97(1H, d, J=8.2 Hz) 6.54(1H, d, J=16.0 Hz) 6.44(1H, s) 6.41(1H, s) 3.93-4.05(3H, m) 3.78(3H, s) 2.80(1H, dd, J=16.3, 5.2 Hz)	Neat 3347 2941 1518 1257	FAB+ 426 [M ⁺ H] ⁺ (34) 154(100)	C ₂₃ H ₂₃ NO ₅ Calcd. C: 70.57% H: 7.34% N: 3.29% Found C: 70.17% H: 7.43% N: 3.23%
1-24		114~ 116°C	CDCl ₃ , 300MHz 7.45(1H, d, J=15.7 Hz) 7.05(1H, dd, J=8.5, 2.2 Hz) 7.01(1H, d, J=2.2 Hz) 6.87(1H, d, J=8.5 Hz) 6.84(1H, d, J=8.5 Hz) 6.70-6.73(2H, m) 6.18(1H, d, J=15.7 Hz) 5.54-5.61(2H, m) 4.01(2H, t, J=6.7 Hz) 3.88(3H, s) 3.87(3H, s) 3.63(2H, q, J=6.7 Hz)	Neat 3244 2930 1516 1258	FAB+ 414 [M ⁺ H] ⁺ (69) 263(58) 247(80) 177(100)	C ₂₄ H ₂₁ NO ₅ Calcd. C: 69.71% H: 7.56% N: 3.39% Found C: 69.73% H: 7.71% N: 3.35%

Table 23

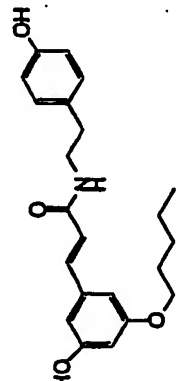
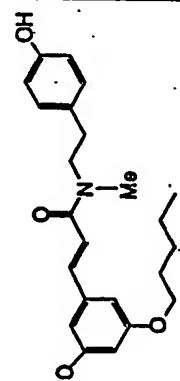
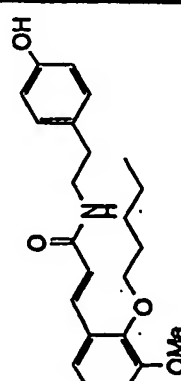
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-25		(dec.) 92.5~ 95.3 °C	DMSO-d ₆ , 300MHz 9.54(1H, s) 9.36(1H, s) 8.30(1H, br) 7.23(1H, d, J=15.8 Hz) 7.00(2H, d, J=8.4 Hz) 6.67(2H, d, J=8.4 Hz) 6.50(1H, d, J=15.8 Hz) 6.50(2H, s) 6.31(1H, s) 3.8-4.0(2H, m) 3.2-3.3(4H, m) 2.5-2.7(2H, m)	KBr 3377 2954 1655 1586	FAB+ 370 [M ⁺ H] ⁺ (40) 163(40)	
1-26			DMSO-d ₆ , 300MHz 9.5(1H, s) 9.2(1H, br) 7.3(1H, d, J=15 Hz) 7.0(1H, d, J=9 Hz) 6.6(1H, d, J=9 Hz) 6.2-6.9(3H, s) 6.0(1H, d, J=15 Hz) 3.9(3H, t, J=7.5 Hz) 3.8-3.9(1H, m) 3.6-3.7(1H, m) 3.4-3.5(1H, m) 3.2-3.4(1H, m)	Neat 3330 2933 2360 2341 1590	FAB+ 384 [M ⁺ H] ⁺ (30)	C ₂₃ H ₂₃ NO ₄ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 71.64% H: 7.74% N: 3.54 %
1-27			CDCl ₃ , 300MHz 7.89(1H, d, J=16 Hz) 6.97-7.10(4H, m) 6.89(1H, dd, J=8.1, 1.8 Hz) 6.80(2H, dd, J=6.6, 1.8 Hz) 6.39(1H, d, J=16 Hz) 5.09-5.15(1H, m) 5.53(1H, s) 3.94(2H, t, J=6.8 Hz) 3.85(3H, s) 3.61(2H, q, J=6.6 Hz) 2.81(2H, t, J=6.9 Hz) 1.70-1.85(2H, m)		FAB+ 384[M+H] ⁺ (100) 177(90)	

Table 24

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-28			CDCl ₃ , 300MHz 9.12(1H, s) 8.99(1H, s) 8.00(1H, t, J=4.1 Hz) 7.25(1H, d, J=11.8 Hz) 7.01(2H, d, J=6.2 Hz) 6.97(1H, s) 6.91(1H, d, J=6.2 Hz) 6.91(1H, d, J=6.2 Hz) 6.68(2H, d, J=6.2 Hz) 6.37(1H, d, J=11.8 Hz) 3.97(2H, t, J=4.9 Hz) 3.3-3.4(2H, m)	KBr 3340 2932 1646 1583	FAB+ 370 [M ⁺ H] ⁺ (40) 233(35)	C ₂₂ H ₂₇ NO ₄ Calcd. C: 71.52% H: 7.37% N: 3.79% Found C: 71.06% H: 7.50% N: 3.74%
1-29			CDCl ₃ , 300MHz 7.57(1H, d, J=15.3 Hz) 7.34(1H, s) 7.32(1H, dd, J=8.2 Hz) 7.06(2H, d, J=8.2 Hz) 6.82(3H, d, J=8.2 Hz) 6.19(1H, br) 6.18(1H, d, J=15.3 Hz) 3.83(2H, t, J=6.9 Hz) 3.61(2H, q, J=6.6 Hz) 2.80(2H, t, J=7.0 Hz) 1.72-1.82(2H, m) 1.32(6H, s)	KBr 3389 3162 1654 1611	FAB+ 424 [M ⁺ H] ⁺ (100) 287(57) 161(53)	C ₂₇ H ₂₇ NO ₃ Calcd. C: 76.56% H: 8.80% N: 3.31% Found C: 76.80% H: 9.18% N: 3.48%
1-30			CDCl ₃ , 300MHz 8.50(1H, d, J=8.35 Hz) 7.59(1H, d, J=15.6 Hz) 7.36(1H, br) 7.32(1H, d, J=5.85 Hz) 7.16(1H, d, J=5.85 Hz) 6.83(1H, d, J=5.85 Hz) 6.23(1H, d, J=15.6 Hz) 5.89(1H, br) 3.84(3H, s) 3.68(2H, q, J=6.56 Hz) 2.91(2H, t, J=7.02 Hz) 1.72-1.83(2H, m)	Neat 3270 1655 1618 1600	FAB+ 409 [M ⁺ H] ⁺ (30) 106(100)	

Table 25

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elen. anal.
1-31			CDCl ₃ , 300MHz 7.50-7.88(1H, bs) 7.55(1H, d, J=15.5 Hz) 7.25-7.34(2H, m) 6.55-6.60(1H, m) 6.21(1H, d, J=15.5 Hz) 5.90(1H, bs) 3.81(3H, s) 3.72(2H, t, J=6.9 Hz) 3.50-3.62(2H, m) 1.72-1.80(2H, m) 1.31(6H, s) 1.08-1.25(6H, m)	KBr 3650- 3000 1651 1598	FAB+ 440 [M ⁺ H ⁺](90) 287(100) 161(77)	
1-32			CDCl ₃ , 300MHz 7.55(1H, d, J=16 Hz) 7.28(1H, d, J=9.6 Hz) 7.27(1H, s) 7.07(2H, d, J=8.4 Hz) 6.81(2H, d, J=8.4 Hz) 6.80(1H, d, J=9.6 Hz) 6.18(1H, d, J=16 Hz) 5.50-5.60(2H, m, involving a singlet at 5.55) 3.83(3H, s) 3.61(2H, q, J=6.6 Hz) 2.81(2H, t, J=6.8 Hz)		FAB+ 382 [M ⁺ H ⁺](80) 260(20) 245(50)	
1-33			CDCl ₃ , 300MHz 8.54(2H, d, J=6.0 Hz) 7.57(1H, d, J=15 Hz) 7.29(1H, d, J=8.7 Hz) 7.28(1H, s) 7.16(2H, d, J=6.0 Hz) 6.81(1H, d, J=8.7 Hz) 6.19(1H, d, J=15 Hz) 5.53-5.61(1H, m) 3.84(3H, s) 3.67(2H, q, J=6.5 Hz) 2.91(2H, t, J=6.9 Hz) 2.58(2H, t, J=7.7 Hz)		FAB+ 367 [M ⁺ H ⁺](90) 245(20)	

Table 26

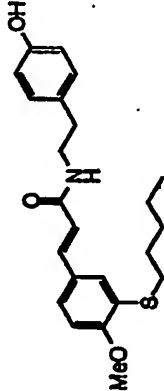
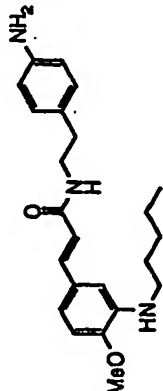
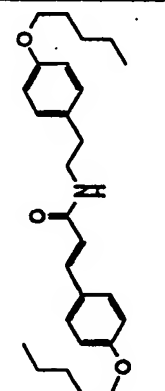
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-34		107.3 ~ 108.5 °C	CDCl ₃ , 300MHz 7.55(1H, d, J=15.4Hz) 7.36(1H, d, J=1.8Hz) 7.29(1H, dd, J=1.8, 8.4Hz) 7.08(1H, d, J=8.4Hz) 6.78-6.84(3H, m) 6.19(1H, d, J=15.4Hz) 3.91(3H, s) 3.62(2H, q, J=6.5Hz) 2.89(2H, t, J=7.2Hz) 2.81(2H, t, J=6.8Hz) 1.58-1.73(2H, m) 1.25-1.50(4H, m)		FAB+ 400[M+H+] (100)	C ₂₃ H ₂₉ NO ₃ S
1-35		143.1 ~ 144.9 °C	CDCl ₃ , 300MHz 7.52(1H, d, J=15 Hz) 7.02(2H, d, J=8.1 Hz) 6.79(1H, d, J=8.1 Hz) 6.71(1H, d, J=8.1 Hz) 6.70(1H, s) 6.66(2H, d, J=8.1 Hz) 6.16(1H, d, J=15 Hz) 5.50(1H, bt) 4.18(1H, bt) 3.86(3H, s) 3.61(2H, bt) 3.60(2H, q, J=6.5 Hz)		FAB+ 382 [M+H] ⁺ (50) 246(20)	
1-36			DMSO-d ₆ , 300MHz 8.0 (1H, bt) 7.5 (2H, d, J=9 Hz) 7.3 (1H, d, J=15 Hz) 7.1 (2H, d, J=9 Hz) 6.9 (2H, d, J=9 Hz) 6.8 (2H, d, J=9 Hz) 6.4 (1H, d, J=15 Hz) 4.0 (2H, t, J=4 Hz) 3.9 (2H, t, J=4 Hz) 3.3 (2H, t, J=4 Hz) 2.7 (2H, t, J=4 Hz) 1.6-1.8 (4H, m)	Neat 3298 2932 1651 1606 1543 1513 1256	FAB+ 424[M+H+] (100)	

Table 27

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRem ⁻¹	MS	Elem. anal.
1-37			DMSO-d ₆ 300MHz 8.0 (1H, bt) 7.3 (1H, d, J=15 Hz) 7.1 (1H, s) 7.1 (2H, d, J=9 Hz) 7.1 (1H, d, J=9 Hz) 6.9 (1H, d, J=9 Hz) 6.8 (2H, d, J=9 Hz) 6.5 (1H, d, J=15 Hz) 3.8-4.0 (4H, m) 3.8 (3H, s) 3.2-3.3 (2H, m) 2.7 (2H, t, J=4 Hz)	Neat 3303 2955 2870 1652 1619 1515 1258	FAB+ 454[M+H+] (100)	
1-38			DMSO-d ₆ 300MHz 9.2 (1H, s) 8.0 (1H, bt) 7.5 (2H, d, J=9 Hz) 7.3 (1H, d, J=15 Hz) 7.0 (2H, d, J=9 Hz) 6.9 (2H, d, J=9 Hz) 6.7 (2H, d, J=9 Hz) 6.4 (1H, d, J=15 Hz) 4.0 (2H, t, J=4 Hz) 3.3 (2H, t, J=4 Hz) 2.6 (2H, t, J=4 Hz) 1.6-1.8 (2H, m)	Neat 3300 2933 2359 1652 1602 1513 1227	FAB+ 354[M+H+] (100)	C ₂₂ H ₂₇ NO ₃ Calcd. C: 74.46% H: 7.70% N: 3.96% Found C: 74.68% H: 7.88% N: 3.98%
1-39			DMSO-d ₆ 300MHz 8.0 (1H, bt) 7.3 (1H, d, J=15 Hz) 7.1 (2H, d, J=9 Hz) 7.0-7.1 (2H, m) 7.0 (1H, d, J=6 Hz) 6.8 (2H, d, J=9 Hz) 6.5 (1H, d, J=15 Hz) 3.8-4.0 (4H, m) 3.8 (3H, s) 3.3-3.5 (2H, m) 2.7 (2H, t, J=4 Hz) 1.6-1.8 (4H, m)	NaCl 3305 2933 1652 1619 1514 1257	FAB+ 454 [M+H+](50)	C ₂₂ H ₂₇ NO ₄ Calcd. C: 74.14% H: 8.67% N: 3.09% Found C: 74.29% H: 8.84% N: 3.16%

Table 28

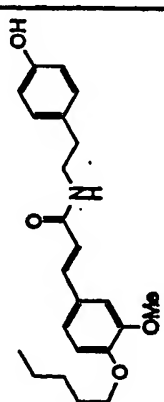
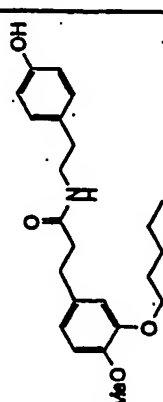
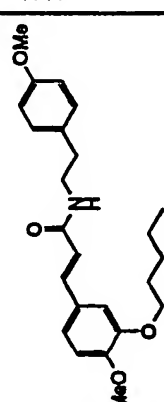
Ex.	Structural formula	n.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-40			DMSO-d ₆ 300MHz 9.1 (1H, s) 7.9 (1H, bs) 7.3 (1H, d, J=15 Hz) 7.1 (1H, s) 7.1 (1H, d, J=6 Hz) 7.0 (2H, d, J=4 Hz) 7.0 (1H, d, J=6 Hz) 6.7 (2H, d, J=4 Hz) 6.5 (1H, d, J=15 Hz) 4.0 (2H, t, J=6 Hz) 3.8 (3H, s) 3.3 (2H, m)	Neat 3462 3312 2938 1648 1600 1540 1512 1263 1138	FAB+ 384 [M+H+] ⁺ (30)	C ₂₃ H ₂₉ NO ₄ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 72.16% H: 7.80% N: 3.65%
1-41		73.8~ 74.1 °C	CDCl ₃ 300MHz 6.92 (2H, d, J=8.5 Hz) 6.77 (1H, d, J=8.1 Hz) 6.76 (2H, d, J=8.5 Hz) 6.71 (1H, d, J=1.9 Hz) 6.68 (2H, dd, J=8.0, 1.9 Hz) 6.50 (1H, s) 5.43 (1H, bs) 3.95 (2H, t, J=6.9 Hz) 3.82 (3H, s) 3.43 (2H, q, J=6.9 Hz) 2.86 (2H, t, J=7.5 Hz)	Neat 3354 2933 1644 1515	FAB+ 386 [M+H+] ⁺ (95) 137(100)	C ₂₃ H ₃₁ NO ₄ Calcd. C: 71.66% H: 8.11% N: 3.63% Found C: 71.64% H: 8.28% N: 3.63%
1-42		116.2~ 117.2 °C	CDCl ₃ 300MHz 7.8 (1H, d, J=15 Hz) 7.2 (2H, d, J=9 Hz) 7.1 (1H, dd, J=9, 1 Hz) 7.0 (1H, d, J=1 Hz) 6.9 (2H, d, J=9 Hz) 6.8 (1H, d, J=9 Hz) 6.2 (1H, d, J=15 Hz) 5.6 (1H, bs) 4.0 (2H, t, J=4 Hz) 3.9 (3H, s) 3.6 (2H, q, J=7 Hz) 2.8 (2H, t, J=7 Hz)	KBr 3293 2934 1650 1614 1511	FAB+ 398 [M+H+] ⁺ (70) 262(60) 177(100)	C ₂₄ H ₃₁ NO ₄ Calcd. C: 72.52% H: 7.86% N: 3.52% Found C: 72.07% H: 7.99% N: 3.56%

Table 29

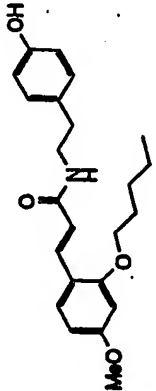
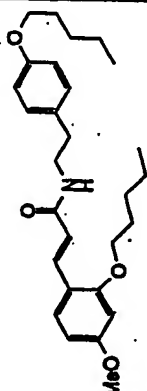
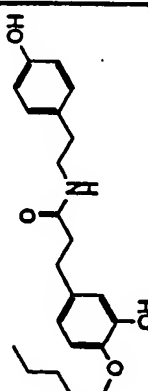
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
1-43			CDCl ₃ 300MHz 7.8 (1H, d, J=15 Hz) 7.4 (1H, d, J=6 Hz) 7.4 (1H, d, J=6 Hz) 7.1 (1H, d, J=8 Hz) 6.8 (1H, d, J=8 Hz) 6.5 (1H, d, J=6 Hz) 6.4 (1H, s) 6.4 (1H, d, J=15 Hz) 5.5 (1H, bt) 5.2 (1H, bs) 4.0 (2H, t, 6 Hz) 3.8 (3H, s)	Neat 3278 2933 1649 1602 1602 1514	FAB+ 384 [M+H] ⁺ (60) 177 (100)	C ₂₃ H ₂₉ NO ₄ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 72.23% H: 7.81% N: 3.60%
1-44						
1-45						

Table 30

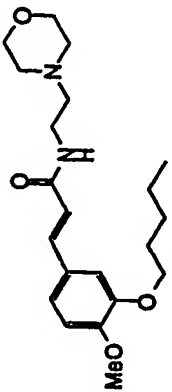
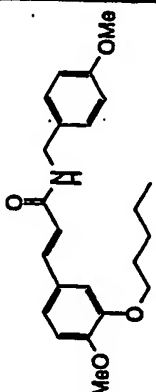
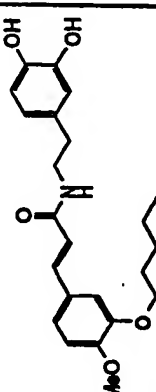
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-46		170.1~ 171.2°C	CDCl ₃ 300MHz 8.3 (1H, br) 7.5 (1H, d, J=18 Hz) 7.0 (2H, d, J=9 Hz) 7.0 (1H, s) 6.8 (1H, d, J=9 Hz) 6.4 (1H, d, J=18 Hz) 4.0-4.2 (4H, m) 4.0 (2H, t, J=7.5 Hz) 3.9-4.0 (2H, m) 3.9 (3H, s) 3.5-3.8 (2H, m) 3.3-3.4 (2H, m)	KBr 3276 2956 1666 1627 1514	FAB+ 377 [M+H] ⁺ (100)	C ₂₁ H ₃₂ N ₂ O ₄ Calcd. C: 66.99% H: 8.57% N: 7.44% Found C: 66.94% H: 8.80% N: 7.43%
1-47						
1-48	 Colorless crystals	150~153 °C	DMSO-d ₆ 300MHz 8.73 (1H, s) 8.62 (1H, s) 7.97 (1H, t, J=5.9 Hz) 7.33 (1H, d, J=16.5 Hz) 7.13 (1H, d, J=2.0 Hz) 7.09 (1H, dd, J=9.0, 2.0 Hz) 6.97 (1H, d, J=9.0 Hz) 6.63 (1H, d, J=9.0 Hz) 6.60 (1H, d, J=2.0 Hz) 6.48 (1H, d, J=9.0 Hz)	3340 1515 1259 1140	FAB+ 400 [M+H] ⁺ (92) 307(14) 247(71) 177(80) 154(100)	

Table 31

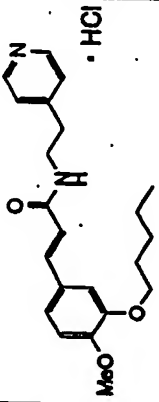
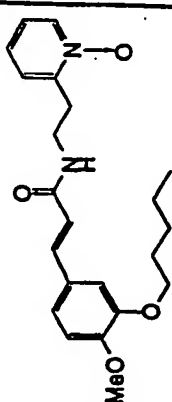
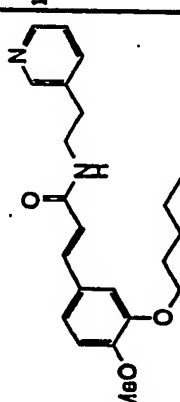
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-49	 <p>Pale-yellow amorphous</p>		CDCl ₃ , 300MHz 8.79 (2H, d, J=6.9 Hz) 8.16 (1H, brt) 7.88 (2H, d, J=6.9 Hz) 7.32 (1H, d, J=15.8 Hz) 7.07-7.12 (2H, m) 6.97 (1H, d, J=8.3 Hz) 6.44 (1H, d, J=15.8 Hz) 3.96 (2H, t, J=6.6 Hz) 3.78 (3H, s) 3.56 (2H, q, J=6.5 Hz) 3.06 (2H, t, J=6.5 Hz) 1.66-1.79 (2H, m)	3250 2933 2528 1261 1136 1023		
1-50	 <p>Colorless crystals</p>	108~110 °C	CDCl ₃ , 300MHz 8.28 (1H, d, J=6.3 Hz) 7.72-7.79 (1H, m) 7.50 (1H, d, J=15.4 Hz) 7.19-7.38 (3H, m) 7.02-7.09 (2H, m) 6.84 (1H, d, J=8.1 Hz) 6.26 (1H, d, J=15.4 Hz) 4.03 (2H, t, J=6.8 Hz) 3.88 (3H, s) 3.72-3.82 (1H, m) 3.28 (2H, t, J=6.3 Hz) 1.80-1.92 (2H, m)	1512 1262	384[M+H] ⁺ (100) 247(89) 177(75)	
1-51	 <p>Colorless crystals</p>	130~132 °C	CDCl ₃ , 300MHz 8.47-8.54 (2H, m) 7.51-7.62 (2H, m) 7.24-7.28 (1H, m) 6.59-7.09 (1H, m) 6.85 (1H, d, J=8.5 Hz) 6.19 (1H, d, J=18.2 Hz) 5.51-5.70 (1H, m) 4.02 (2H, t, J=7.3 Hz) 3.89 (1H, s) 3.66 (2H, q, J=6.9 Hz) 2.91 (2H, t, J=6.9 Hz) 1.80-1.92 (2H, m)	3245 1596 1263 1140	FAB+ 369[M+H] ⁺ (100) 311(21) 247(14) 177(29)	

Table 32

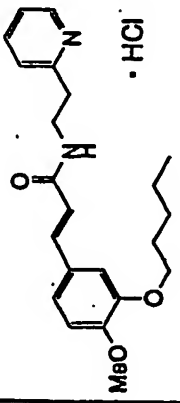
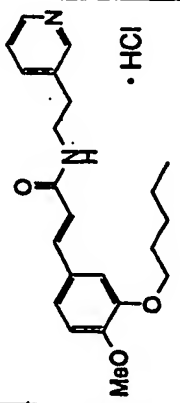
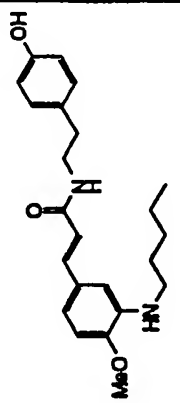
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-52						
1-53						
1-54	 Yellow crystals	162.7 ~ 163.5 °C	CDCl ₃ , 300MHz 7.53(1H, d, J=15 Hz) 7.31(2H, d, J=8.7 Hz) 6.75-6.85(3H, m) 6.71(1H, d, J=8.1 Hz) 6.70(1H, s) 6.17(1H, d, J=15 Hz) 5.58(1H, bs) 5.58(1H, bs) 4.2(1H, bs) 3.86(3H, s) 3.61(2H, q, J=6.4 Hz) 3.12(2H, t, J=7.2 Hz)		FAB+ 383 [M ⁺ H] ⁺ (50) 246(60)	

Table 33

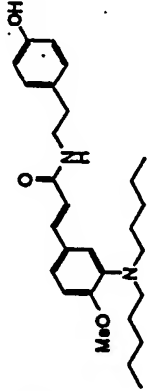
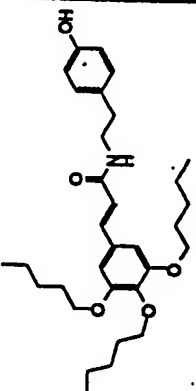
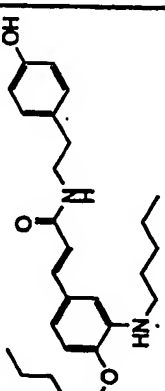
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-55			CDCl ₃ , 300MHz 7.54(1H, d, J=16 Hz) 7.03-7.12(4H, m) 6.81(1H, d, J=8.4 Hz) 6.80(2H, d, J=8.1 Hz) 6.17(1H, d, J=16 Hz) 5.56(1H, br) 3.86(3H, s) 3.61(2H, q, J=6.3 Hz) 3.06(4H, t, J=7.7 Hz) 2.81(2H, t, J=6.8 Hz) 1.38-1.5(4H, m) 1.07-1.35(8H, m)		FAB+ 453 [M ⁺ H] ⁺ (100) 395(80)	
1-56	 Colorless crystals	144.9~ 145.5°C	CDCl ₃ , 300MHz 7.50(1H, d, J=15 Hz) 7.08(2H, d, J=8.4 Hz) 6.80(2H, d, J=8.4 Hz) 6.67(2H, s) 6.19(1H, d, J=15 Hz) 5.58(1H, br) 5.49(1H, s) 3.97(6H, t, J=6.5 Hz) 3.62(2H, q, J=6.5 Hz) 2.81(2H, t, J=6.8 Hz) 1.7-1.85(6H, m) 1.3-1.5(12H, m)		FAB+ 526 [M ⁺ H] ⁺ (30) 389(40)	
1-57	 Colorless crystals	119.9~ 121.3°C	CDCl ₃ , 300MHz 7.54(1H, d, J=16 Hz) 7.07(2H, d, J=8.4 Hz) 6.80(2H, d, J=8.4 Hz) 6.77(1H, dd, J=8.7, 2.1 Hz) 6.70(1H, s) 6.69(1H, d, J=8.7 Hz) 6.17(1H, dd, J=16 Hz) 5.8(1H, br) 5.58(1H, br) 4.00(2H, t, J=6.6 Hz) 3.61(2H, q, J=6.6 Hz) 3.12(2H, t, J=7.1 Hz)		FAB+ 439 [M ⁺ H] ⁺ (50) 302(100)	

Table 34

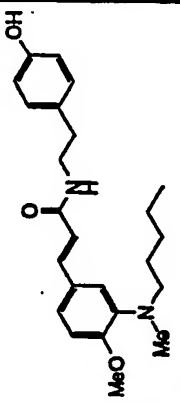
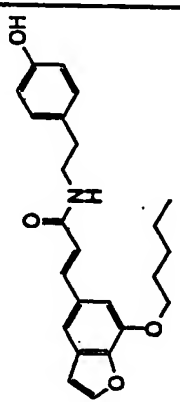
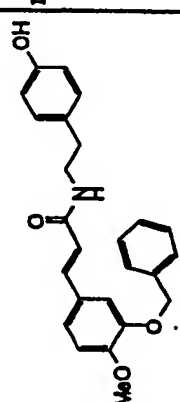
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-58	 <p>Colorless crystals</p>	104.8~ 106.4 °C	CDCl ₃ , 300MHz 7.55(1H, d, J=16Hz) 7.02-7.12(4H, m) 6.77-6.85(3H, m) 6.17(1H, d, J=16 Hz), 5.58(1H, brt) 3.88(3H, s) 3.61(2H, q, J=6.5 Hz) 3.02(2H, t, J=8.0 Hz) 2.81(2H, t, J=6.9 Hz) 2.78(3H, s) 1.5-1.65(2H, m) 1.22-1.48(4H, m)		FAB+ 397 [M+H] ⁺ (100) 39(80)	
1-59	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.67 (1H, d, J=15.4 Hz) 7.62 (1H, d, J=2.2 Hz) 7.30 (1H, d, J=1.5 Hz) 7.06-7.09 (2H, m) 6.92 (1H, d, J=1.5 Hz) 6.81-6.84 (2H, m) 6.73 (1H, d, J=2.2 Hz) 6.27 (1H, d, J=15.4 Hz) 5.95 (1H, s) 5.67 (1H, brt) 4.17 (2H, t, J=6.6 Hz) 3.63 (2H, q, J=6.6 Hz)	2953 1656 1606 1516 1339 1150	FAB+ 394 [M+H] ⁺ (73) 187(100)	C ₂₄ H ₂₇ NO ₄ Calcd. C: 73.26% H: 6.92% N: 3.56% Found C: 73.25% H: 6.96% N: 3.56%
1-60	 <p>Colorless crystals</p>	161~162 °C	CDCl ₃ , 300MHz 7.26-7.52 (6H, m) 7.03-7.08 (4H, m) 6.79-6.88 (3H, m) 6.10 (1H, d, J=15.4) 5.49-5.60 (2H, m) 5.14 (2H, s) 3.90(3H, s) 3.60 (2H, q, J=6.6 Hz) 2.80 (2H, t, J=6.8 Hz)		FAB+ 404 [M+H] ⁺ (32) 154(100)	

Table 35

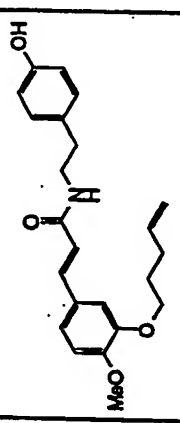
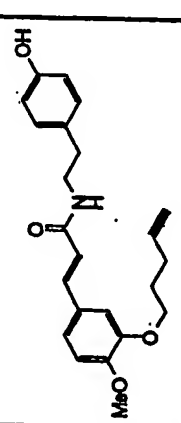
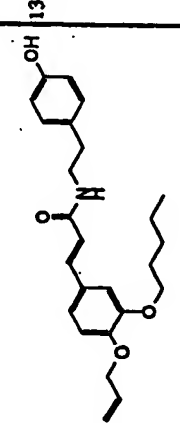
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-61						
1-62						
1-63	 Colorless crystals	132~133 °C	CDCl ₃ 300MHz 7.53 (1H, d, J=15.5 Hz) 1.80-1.87 (2H, m) 6.99-7.06 (4H, m) 1.39-1.49 (4H, m) 6.79-6.84 (3H, m) 0.92 (3H, t, J=7.1 Hz) 6.31 (1H, s) 6.18 (1H, d, J=15.5 Hz) 5.99-6.11 (1H, m) 5.68 (1H, br) 5.25-5.44 (2H, m) 4.59 (2H, m) 3.99 (2H, t, J=6.7 Hz) 3.60 (2H, q, J=6.7 Hz) 2.79 (2H, t, J=6.7 Hz)		FAB+ 410(M+H+) (100) 288(25) 273(35)	

Table 36

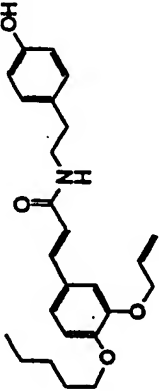
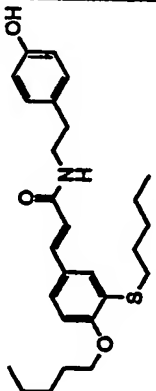
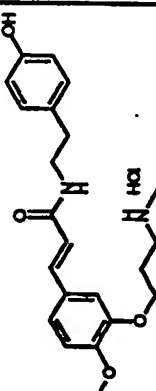
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-64	 <p>Colorless crystals</p>	119~120 °C	CDCl ₃ 300MHz 7.52 (1H, d, J=15.4 Hz) 1.79-1.86 (2H, m) 7.02-7.09 (4H, m) 1.38-1.48 (4H, m) 6.79-6.86 (3H, m) 0.93 (3H, t, J=7.0 Hz) 6.15 (1H, d, J=15.4 Hz) 6.01-6.12 (1H, m) 5.55 (1H, brt) 5.34 (1H, s) 5.26-5.45 (2H, m) 4.58-4.61 (2H, m) 4.02 (2H, t, J=6.9 Hz) 3.61 (2H, q, J=6.7 Hz) 2.81 (1H, t, J=6.7 Hz)		FAB+ 410 [M+H] ⁺ (77) 273(36) 154(100)	
1-65	 <p>Colorless crystals</p>	109.5~ 110.4 °C	CDCl ₃ 300MHz 7.53 (1H, d, J=15.5 Hz) 2.81 (2H, t, J=6.9 Hz) 7.36 (1H, d, J=2.1 Hz) 1.80-1.90 (2H, m) 7.26 (1H, dd, J=2.1, 8.4 Hz) 1.60-1.70 (2H, m) 7.08 (2H, d, J=8.5 Hz) 1.25-1.35 (8H, m) 6.80 (2H, d, J=8.5 Hz) 0.93 (3H, t, J=7.1 Hz) 6.79 (1H, d, J=8.4 Hz) 0.90 (3H, t, J=7.1 Hz) 6.17 (1H, d, J=15.5 Hz) 5.54 (1H, br) 5.14 (1H, s) 4.03 (2H, t, J=6.6 Hz) 3.61 (2H, t, J=6.6 Hz) 2.88 (2H, t, J=7.4 Hz)		FAB+ 456 [M+H] ⁺ (100) 319 (50)	C ₂₇ H ₃₇ N ₃ O ₃
1-66	 <p>Yellow crystals</p>	221~222 °C	DMSO-d ₆ 300MHz 8.97 (2H, br) 3.31 (2H, q, J=6.6 Hz) 8.63 (1H, br) 2.9-3.1 (2H, m) 8.05 (1H, t, J=5.7 Hz) 2.63 (2H, t, J=7.5 Hz) 7.31 (1H, d, J=15.6 Hz) 2.55 (3H, t, J=6.0 Hz) 7.15 (1H, d, J=1.8 Hz) 2.0-2.2 (2H, m) 7.12 (1H, dd, J=8.4, 1.8 Hz) 6.99 (2H, d, J=8.4 Hz) 6.99 (1H, d, J=8.4 Hz) 6.67 (2H, d, J=8.4 Hz) 6.52 (1H, d, J=15.6 Hz) 4.08 (2H, t, J=6.6 Hz) 3.78 (3H, s)	KBr 3215 1653 1617 1516	FAB+ 385 [M+H] ⁺ (80), 154 (100), 136 (80).	C ₂₂ H ₂₈ N ₂ O ₄ ·HCl Calcd. C: 62.77% H: 6.70% N: 6.65% Found C: 57.75% H: 6.75% N: 6.05%

Table 37

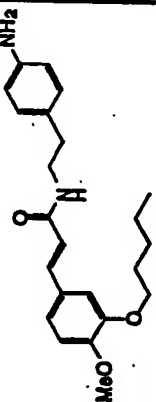
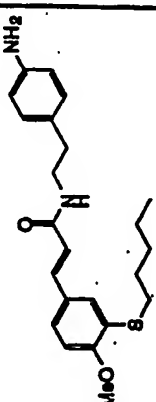
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-68	 <p>Colorless crystals</p>	139.7~ 142.3°C	CDCl ₃ , 300MHz 7.53(1H, d, J=16 Hz) 7.05(1H, d, J=8.4 Hz) 7.02(2H, d, J=8.4 Hz) 7.00(1H, s) 6.84(1H, d, J=8.4 Hz) 6.66(2H, d, J=8.4 Hz) 6.16(1H, d, J=16 Hz) 5.50(1H, br) 4.02(2H, t, J=6.8 Hz) 3.88(3H, s) 3.60(2H, br) 3.60(2H, q, J=6.5 Hz)		FAB+ 383 [M ⁺ H ⁺](40) 247(80)	
1-69	 <p>Colorless crystals</p>	113.2~ 116.3°C	CDCl ₃ , 300MHz 7.53(1H, d, J=16 Hz) 7.37(1H, d, J=2.1 Hz) 7.27(1H, d, J=8.5 Hz) 7.01(2H, d, J=8.3 Hz) 6.81(1H, d, J=8.5 Hz) 6.66(2H, d, J=8.3 Hz) 6.17(1H, d, J=16 Hz) 5.53(1H, br) 3.91(3H, s) 3.61(2H, br) 3.60(2H, q, J=6.5 Hz) 2.89(2H, t, J=7.4 Hz)		FAB+ 399 [M ⁺ H ⁺](50) 263(40)	

Table 38

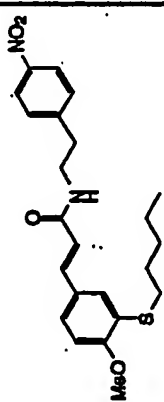
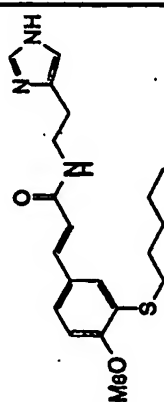
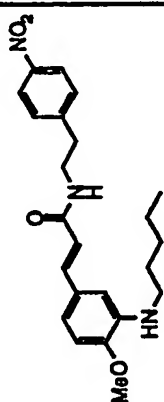
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm⁻¹}	MS	Elem. anal.
1-70	 <p>Pale-yellow crystals</p>	114.1 ~ 114.6 °C	CDCl ₃ , 300MHz 8.20(2H, d, J=8.7 Hz) 7.58(1H, d, J=16 Hz) 7.41(2H, d, J=8.7 Hz) 7.39(1H, d, J=2.4 Hz) 7.31(1H, dd, J=2.1, 8.4 Hz) 6.84(1H, d, J=16 Hz) 5.64(1H, br) 3.93(3H, s) 3.70(2H, q, J=6.9 Hz) 3.04(2H, t, J=7.0 Hz) 2.90(2H, t, J=7.4 Hz) 1.58-1.75(2H, m)		FAB+ 429 [M ⁺ H] ⁺ (20) 307(20)	
1-71	 <p>Colorless crystals</p>	119.2 ~ 120.4 °C	CDCl ₃ , 300MHz 7.60(1H, s) 7.54(1H, d, J=16 Hz) 7.38(1H, d, J=2.1 Hz) 7.30(1H, dd, J=2.1, 8.5 Hz) 6.83(1H, s) 6.82(1H, d, J=8.5 Hz) 6.56(1H, br) 6.28(1H, d, J=16 Hz) 3.91(3H, s) 3.69(2H, q, J=6.9 Hz) 2.83-2.92(4H, m) 1.6-1.73(2H, m)	1.3-1.5(4H, m) 0.90(3H, t, J=7.1 Hz)	FAB+ 374 [M ⁺ H] ⁺ (100) 263(30)	
1-72	 <p>Colorless crystals</p>	122.1 ~ 122.7 °C	CDCl ₃ , 300MHz 8.18(2H, d, J=8.6 Hz) 7.54(1H, d, J=15 Hz) 7.39(2H, d, J=8.6 Hz) 6.80(1H, d, J=8.2 Hz) 6.71(1H, d, J=8.2 Hz) 6.70(1H, s) 6.17(1H, d, J=15 Hz) 5.35(1H, br) 4.20(1H, br) 3.87(3H, s) 3.68(2H, q, J=6.7 Hz) 3.12(2H, q, J=5.7 Hz)	3.02(2H, t, J=6.9 Hz) 1.6-1.73(2H, m) 1.3-1.5(4H, m) 0.93(3H, t, J=7.1 Hz)	FAB+ 412 [M ⁺ H] ⁺ (30) 246(30)	

Table 39

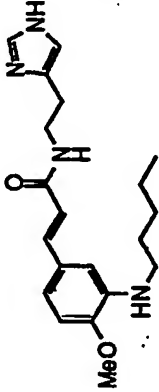
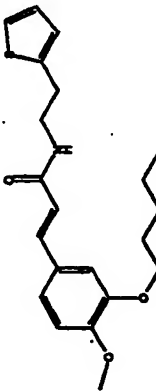
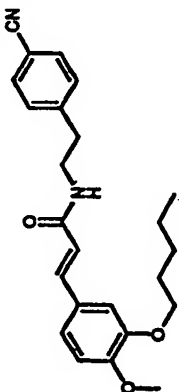
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
1-73	 <p>Colorless crystals</p>	150.7~ 151.6°C	CDCl ₃ , 300MHz 7.55(1H, s) 7.48(1H, d, J=15 Hz) 6.80(1H, s) 6.67(1H, s) 6.66(1H, d, J=8.0 Hz) 6.32(1H, s) 6.19(1H, d, J=15 Hz) 4.12(1H, br) 3.81(3H, s) 3.63(2H, q, J=6.1 Hz) 3.08(2H, br) 2.83(2H, t, J=6.3 Hz)		FAB+ 357 [M ⁺ H] ⁺ (50) 246(30)	
1-74	 <p>Colorless needles</p>	100.6~ 101.2°C	CDCl ₃ , 300MHz 7.55(1H, d, J=16.0 Hz) 7.18(1H, dd, J=5.1, 1.1 Hz) 7.06(1H, dd, J=8.2, 1.9 Hz) 7.01(1H, d, J=1.9 Hz) 6.96(1H, dd, J=5.1, 3.5 Hz) 6.86(1H, dd, J=3.5, 1.5 Hz) 6.84(1H, d, J=8.3 Hz) 6.20(1H, d, J=16.0 Hz) 5.70(1H, br) 4.01(2H, t, J=6.9 Hz) 3.88(3H, s) 3.67(2H, q, J=6.4 Hz)		FAB+ 374[M+H] ⁺ (100)	C ₂₁ H ₂₇ NO ₃ S Calcd. C: 67.53% H: 7.29% N: 3.75% Found C: 67.51% H: 7.47% N: 3.77%
1-75	 <p>Pale-yellow flakes</p>	69.8~ 70.2°C	CDCl ₃ , 300MHz 7.60(2H, d, J=8.4 Hz) 7.55(1H, d, J=15.6 Hz) 7.34(2H, d, J=8.4 Hz) 7.06(1H, dd, J=8.1, 2.1 Hz) 7.00(1H, d, J=2.1 Hz) 6.84(1H, d, J=8.1 Hz) 6.19(1H, d, J=15.6 Hz) 5.64(1H, br) 4.00(2H, t, J=6.6 Hz) 3.88(3H, s) 3.65(2H, q, J=6.9 Hz) 2.95(2H, t, J=6.9 Hz)	KBr 3280 2936 2856 2229 1651 1609 1518 1262	FAB+ 393[M+H] ⁺ (100)	

Table 40

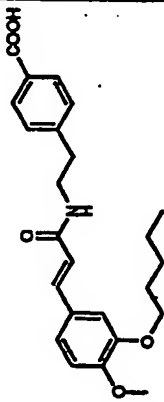
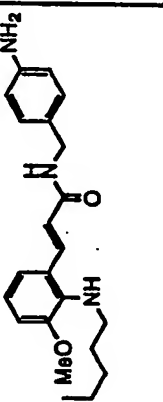
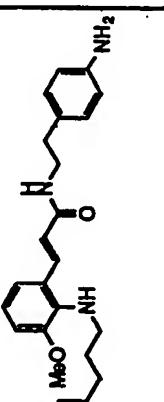
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS.	Elem. anal.
1-76	 <p>Colorless crystals</p>	174.2~ 175.1°C	DMSO-d6, 300MHz 9.0 (1H, bs) 8.04 (1H, bt) 7.87 (2H, d, J = 8.1 Hz) 7.36 (2H, d, J = 8.1 Hz) 7.30 (1H, d, J = 15.7 Hz) 7.13 (1H, d, J = 1.7 Hz) 7.08 (1H, dd, J = 8.3, 1.7 Hz) 6.46 (1H, d, J = 15.7 Hz) 3.97 (2H, t, J = 6.6 Hz) 3.78 (3H, s) 3.44 (2H, q, J = 6.9 Hz) 2.85 (2H, t, J = 6.9 Hz)	KBr 3422 2938 1610 1518 1262	FAB+ 412[M+H+] (100)	
1-77	 <p>Colorless oil</p>		CDCl3, 300MHz 7.89 (1H, d, J = 15.3 Hz) 7.13 (2H, d, J = 8.4 Hz) 7.00 (1H, dd, J = 2.1, 7.2 Hz) 6.75-6.85 (2H, m) 6.66 (2H, d, J = 8.4 Hz) 6.28 (1H, d, J = 15.3 Hz) 5.71 (1H, bt) 4.45 (2H, d, J = 5.4 Hz) 3.84 (3H, s) 3.65 (1H, bt) 3.08 (2H, t, J = 6.9 Hz) 1.45-1.60 (2H, m)			C22H29N3O2
1-78	 <p>Colorless oil</p>		CDCl3, 300MHz 7.84 (1H, d, J = 15.3 Hz) 6.97-7.04 (3H, m) 6.75-6.85 (2H, m) 6.66 (2H, d, J = 8.4 Hz) 6.22 (1H, d, J = 15.3 Hz) 5.56 (1H, bt) 3.84 (3H, s) 3.63 (1H, bt) 3.60 (2H, q, J = 6.6 Hz) 3.07 (2H, t, J = 7.1 Hz) 2.77 (2H, t, J = 6.8 Hz) 1.45-1.60 (2H, m)			C23H31N3O2

Table 41

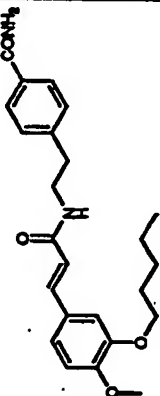
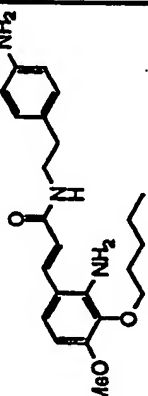
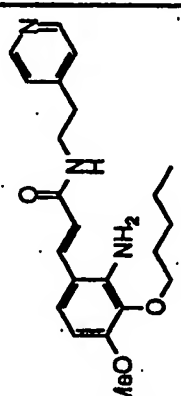
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-79	 <p>Colorless crystals</p>	125.5~ 126.2°C	CDCl ₃ 300MHz 8.04 (1H, br) 7.91 (1H, d, J = 15.9 Hz) 7.75 (2H, d, J = 8.4 Hz) 7.34 (1H, s) 7.28 (2H, d, J = 8.4 Hz) 7.06 (1H, d, J = 8.4 Hz) 6.95 (1H, d, J = 8.4 Hz) 6.46 (1H, d, J = 15.9 Hz) 6.00 (2H, br) 3.96 (2H, t, J = 6.9 Hz) 3.98 (3H, s) 3.4-3.5 (2H, m)	KBr 3440 1684 1214 1138	FAB+ 411[M+H+] (100)	
1-80	 <p>Pale-yellow crystals</p>	130.0~ 131.6°C	CDCl ₃ 300MHz 7.69 (1H, d, J = 15.3 Hz) 7.06 (1H, d, J = 8.8 Hz) 7.01 (2H, d, J = 8.4 Hz) 6.66 (2H, d, J = 8.4 Hz) 6.35 (1H, d, J = 8.8 Hz) 6.13 (1H, d, J = 15.3 Hz) 5.49 (1H, br) 4.21 (2H, br) 3.94 (2H, t, J = 6.8 Hz) 3.84 (3H, s) 3.61 (2H, br) 3.59 (2H, q, J = 6.5 Hz)	KBr 3292 2931 1649 1611 1516 1293 1235 1097	FAB+ 398 [M+H+] (35) 262(40)	C23H31N3O3
1-81	 <p>Pale-yellow crystals</p>	105.8~ 106.9°C	CDCl ₃ 300MHz 8.53 (2H, d, J = 6.0 Hz) 7.70 (1H, d, J = 15.3 Hz) 7.16 (2H, d, J = 6.0 Hz) 7.07 (1H, d, J = 8.8 Hz) 6.35 (1H, d, J = 8.8 Hz) 6.16 (1H, d, J = 15.3 Hz) 5.60 (1H, br) 4.20 (2H, br) 3.94 (2H, t, J = 6.8 Hz) 3.84 (3H, s) 3.67 (2H, q, J = 6.6 Hz) 2.90 (2H, t, J = 6.9 Hz)	KBr 3337 2952 1657 1608 1519 1458 1096	FAB+ 384[M+H+] (100)	C22H29N3O3

Table 42

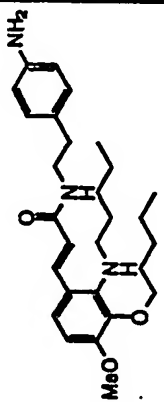
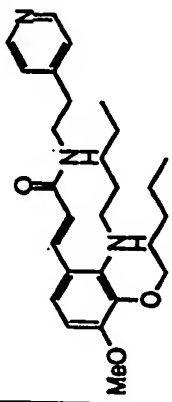
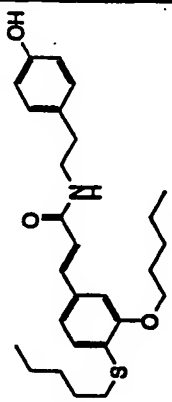
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-82	 <p>Pale-yellow amorphous</p>		CDCl ₃ , 300MHz 7.75(1H, d, J=15.5Hz) 7.09(1H, d, J=8.8Hz) 7.01(2H, d, J=8.3Hz) 6.66(2H, d, J=8.3Hz) 6.45(1H, d, J=8.8Hz) 6.14(1H, d, J=15.5Hz) 5.51(1H, bs) 3.92(2H, t, J=6.7Hz) 3.84(3H, s) 3.62(2H, bs) 3.59(2H, q, J=6.5Hz) 3.08(2H, t, J=7.1Hz)	KBr 3290 2992 1645 1602 1515 1292 1231	FAB+ 468 [M+H] ⁺ (20) 332(20) 262(60)	C ₂₈ H ₄₁ N ₃ O ₃
1-83	 <p>Pale-yellow crystals</p>	68.4~ 69.6°C	CDCl ₃ , 300MHz 8.53(2H, d, J=5.7Hz) 7.78(1H, d, J=15.9Hz) 7.16(2H, d, J=5.7Hz) 7.09(1H, d, J=8.7Hz) 6.46(1H, d, J=8.7Hz) 6.16(1H, d, J=15.9Hz) 5.60(1H, bs) 3.92(2H, t, J=6.8Hz) 3.84(3H, s) 3.66(2H, q, J=6.7Hz) 3.08(2H, t, J=7.1Hz) 2.90(2H, t, J=7.1Hz)	KBr 3294 2936 1648 1604 1550 1292 1232 1106	FAB+ 454[M+H] ⁺ (100)	C ₂₇ H ₃₉ N ₃ O ₃
1-84	 <p>Colorless crystals</p>	107.3~ 109.5°C	CDCl ₃ , 300MHz 7.54(1H, d, J=15 Hz) 7.14(1H, d, J=8.1 Hz) 7.08(2H, d, J=8.3 Hz) 7.03(1H, d, J=8.1 Hz) 6.90(1H, s) 6.80(2H, d, J=8.3 Hz) 6.24(1H, d, J=15 Hz) 5.55(1H, bs) 5.00(1H, bs) 4.02(2H, t, J=6.6 Hz) 3.62(2H, q, J=6.1 Hz) 2.85(2H, t, J=7.4 Hz)		FAB+ 456 [M+H] ⁺ (100) 319(60)	

Table 43

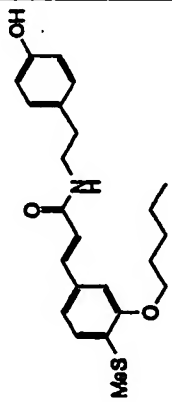
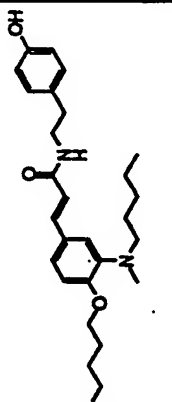
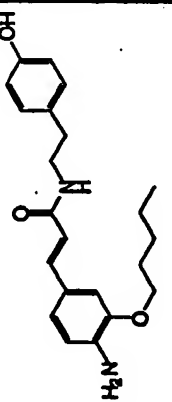
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
1-85	 <p>Colorless crystals</p>	140.3 ~ 140.9 °C	CDCl ₃ , 300MHz 7.55(1H, d, J=16 Hz) 7.06-7.13(4H, m) 6.90(1H, s) 6.80(2H, d, J=8.5 Hz) 6.24(1H, d, J=16 Hz) 5.54(1H, t) 4.97(1H, t) 4.03(2H, t, J=6.5 Hz) 3.62(2H, q, J=6.1 Hz) 2.81(2H, t, J=6.9 Hz) 2.43(3H, s) 1.8-1.9(2H, m)		FAB+ 400 [M ⁺ H] ⁺ (40) 307(100)	
1-86	 <p>Colorless crystals</p>	113.9-114.5 °C	CDCl ₃ , 300MHz 7.54(1H, d, J=15.5 Hz) 7.08(2H, d, J=8.5 Hz) 7.07(1H, d, J=8.45 Hz) 7.03(1H, s) 6.80(2H, d, J=8.5 Hz) 6.79(1H, d, J=8.4 Hz) 6.17(1H, d, J=15.5 Hz) 5.53(1H, t) 5.17(1H, s) 4.01(2H, t, J=6.6 Hz) 3.61(2H, q, J=6.6 Hz) 3.04(2H, t, J=7.8 Hz)		FAB+ 453[M+H] ⁺ (100) 395(90) 316(50)	C28H40N2O3
1-87	 <p>Colorless crystals</p>		DMSO-d ₆ , 300MHz 9.14(1H, s) 7.84(1H, t, J=5.7 Hz) 7.23(1H, d, J=15.6 Hz) 6.99(1H, d, J=8.4 Hz) 6.94(1H, s) 6.87(1H, d, J=8.1 Hz) 6.66(2H, d, J=8.4 Hz) 6.60(1H, d, J=8.1 Hz) 6.19(1H, d, J=15.6 Hz) 5.11(2H, t) 3.95(2H, t, J=6.6 Hz) 3.25-3.34(5H, m)		FAB+ 369 [M+H] ⁺ (80) 368(80)	

Table 44

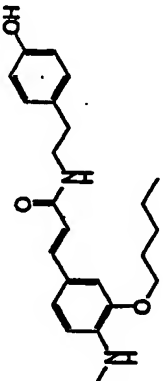
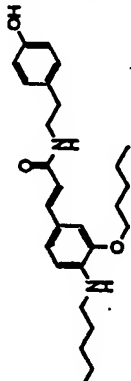
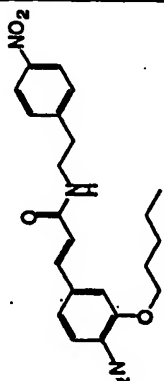
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-88	 <p>Pale-yellow crystals</p>	213.7~ 214.7°C	CDCl ₃ 300MHz 7.52(1H, d, J=15 Hz) 7.09(2H, d, J=8.5 Hz) 7.03(1H, d, J=8.1 Hz) 6.87(1H, s) 6.79(2H, d, J=8.5 Hz) 6.51(1H, d, J=8.1 Hz) 6.08(1H, d, J=15 Hz) 5.47(1H, bt) 4.98(1H, s) 4.51(1H, bs) 3.99(2H, t, J=6.5 Hz) 3.61(2H, q, J=6.2 Hz)		FAB+ 337 [M+H+] ⁺ (50) 246(30)	C ₂₃ H ₃₀ N ₂ O ₃
1-89	 <p>Colorless crystals</p>		CDCl ₃ 300MHz 7.51(1H, d, J=15.4Hz) 7.08(2H, d, J=8.4Hz) 7.01(1H, d, J=8.2Hz) 6.87(1H, s) 6.79(2H, d, J=8.4Hz) 6.51(1H, d, J=8.2Hz) 6.06(1H, d, J=15.4Hz) 5.45(1H, bt) 4.99(1H, s) 4.49(1H, bs) 3.99(2H, t, J=6.5Hz) 3.60(2H, q, J=6.5Hz)		FAB+ 438 [M+H+] ⁺ (30) 302(30)	C ₂₇ H ₂₈ N ₂ O ₃
1-90	 <p>Pale-yellow crystals</p>		CDCl ₃ 300MHz 7.52(1H, d, J=15.5Hz) 7.02(2H, d, J=8.3Hz) 6.63-6.81(5H, m) 6.16(1H, d, J=15.5Hz) 5.53(1H, bt) 3.66-3.75(2H, m) 3.59(2H, q, J=6.5Hz) 3.13(2H, bs) 2.77(2H, t, J=6.8Hz) 1.60-1.75(2H, m) 1.30-1.50(4H, m) 0.93(3H, t, J=7.1Hz)			

Table 45

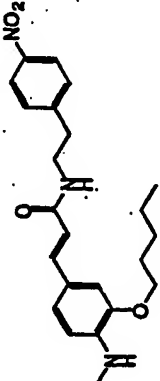
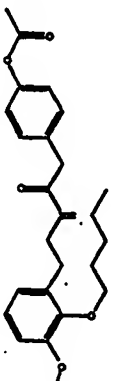
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
1-91	 <p>Pale-orange crystals</p>	136.5-137.0°C	CDCl ₃ , 300MHz 8.17(2H, d, J=8.7 Hz) 7.52(1H, d, J=15 Hz) 7.38(2H, d, J=8.7 Hz) 7.03(1H, d, J=8.2 Hz) 6.86(1H, s) 6.50(1H, d, J=8.2 Hz) 6.07(1H, d, J=15 Hz) 5.47(1H, br) 4.55(1H, br) 3.98(2H, t, J=6.5 Hz) 3.66(2H, q, J=6.6 Hz) 3.00(2H, t, J=6.9 Hz)		FAB+ 412 [M+H] ⁺ (20) 246(50)	C ₂₃ H ₂₉ N ₃ O ₄
1-92	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 7.10(2H, d, J=8.5 Hz) 7.00(2H, d, J=8.5 Hz) 6.93(2H, t, J=7.9 Hz) 6.77(1H, d, J=7.9 Hz) 6.63(1H, d, J=7.9 Hz) 5.80(1H, br) 3.91(2H, t, J=6.7 Hz) 3.84(3H, s) 3.47(2H, s) 3.45(2H, q, J=6.2 Hz) 2.78(2H, t, J=6.2 Hz) 2.29(3H, s)		FAB+ 414[M+H] ⁺ (100)	

Table 46

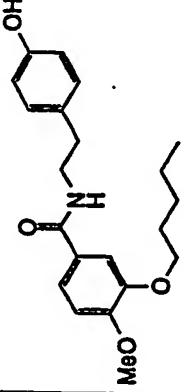
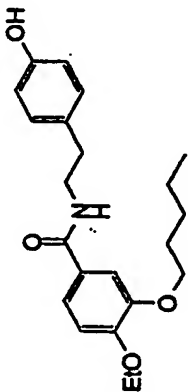
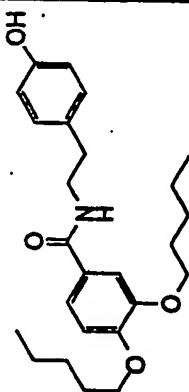
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-1		114.3 ~ 115.6 °C	CDCl ₃ 300MHz 7.35(1H, d, J=2.0 Hz) 7.15(1H, dd, J=8.3, 2.0 Hz) 7.03(2H, d, J=8.4 Hz) 6.80(2H, d, J=8.4 Hz) 6.80(1H, d, J=8.3 Hz) 6.62(1H, br) 6.19(1H, br) 3.98(2H, t, J=6.9 Hz) 3.86(3H, s) 3.64(2H, q, J=6.9 Hz) 2.82(2H, t, J=6.9 Hz) 1.7-1.9(2H, m)	KBr 3322 1633	FAB+ 358 [M ⁺ H] ⁺ (100) 221(100)	C ₁₁ H ₁₇ NO ₄ Calcd. C; 70.56% H; 7.61% N; 3.92% Found C; 70.58% H; 7.79% N; 3.89 %
2-2		116 ~ 117 °C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.33(1H, t) 7.39-7.41(2H, m) 6.96-7.02(3H, m) 6.66(2H, d, J=8.4 Hz) 4.05(2H, q, J=6.9 Hz) 3.97(2H, t, J=6.6 Hz) 3.32-3.43(2H, m) 2.69(2H, t, J=7.5 Hz) 1.66-1.78(2H, m) 1.28-1.47(7H, m) 0.89(3H, t, J=7.2 Hz)		FAB+ 372 [M ⁺ H] ⁺ (55) 235(100) 206(24) 164(23)	
2-3		134 ~ 136 °C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.33(1H, t, J=5.4 Hz) 7.40-7.42(2H, m) 6.97-7.03(3H, m) 6.68(2H, d, J=8.4 Hz) 3.96-4.01(4H, m) 3.32-3.45(2H, m) 2.70(2H, t, J=7.4 Hz) 1.64-1.78(4H, m) 1.26-1.49(8H, m) 0.83-0.94(6H, m)		FAB+ 414 [M ⁺ H] ⁺ (100) 277(58) 207(59) 170(75) 136(85)	

Table 47

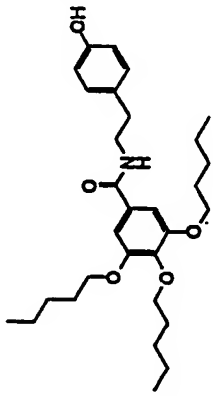
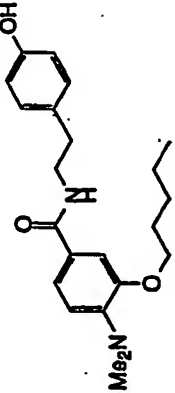
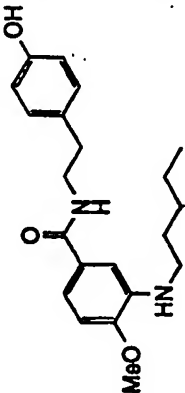
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm} ⁻¹	MS	Elem. anal.
2-4	 <p>Colorless crystals</p>	93.6~ 94.2°C	CDCl ₃ , 300MHz 7.09(2H, d, J=8.4 Hz) 6.86(2H, s) 6.79(2H, dd, J=8.4, 2.1 Hz) 6.0(1H, br) 3.92-4.03(6H, m) 3.64(2H, q, J=6.6 Hz) 2.84(2H, t, J=7.1 Hz) 1.7-1.88(6H, m) 1.3-1.5(12H, m) 0.88-1.0 (12H, m)		FAB+ 500 [M ⁺ H] ⁺ (70) 293(65)	
2-5	 <p>Colorless crystals</p>	95.3~ 96.4°C	CDCl ₃ , 300MHz 7.33(1H, s) 7.09(2H, d, J=8.4 Hz) 7.08(1H, d, J=8.1 Hz) 6.8(1H, d, J=8.1 Hz) 6.79(2H, d, J=8.4 Hz) 6.05(1H, br) 5.33(1H, bs) 4.03(2H, t, J=6.6 Hz) 3.65(2H, q, J=6.6 Hz) 2.86(6H, s) 2.85(2H, t, J=6.9 Hz) 1.8-1.9(2H, m)		FAB+ 371 [M ⁺ H] ⁺ (100) 234(50)	
2-6	 <p>Colorless crystals</p>	145.9~ 146.5°C	CDCl ₃ , 300MHz 7.09(2H, d, J=8.4 Hz) 6.98(1H, d, J=1.8 Hz) 6.91(1H, dd, J=7.8, 2.1 Hz) 6.79(2H, d, J=8.4 Hz) 6.70(1H, d, J=7.8 Hz) 6.04(1H, br) 5.30(1H, br) 4.11(1H, br) 3.87(3H, s) 3.65(2H, q, J=6.6 Hz) 3.13(2H, t, J=7.1 Hz) 2.85(2H, t, J=6.9 Hz)		FAB+ 357 [M ⁺ H] ⁺ (100) 220(80)	

Table 48

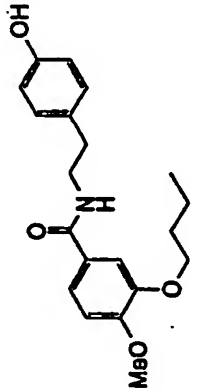
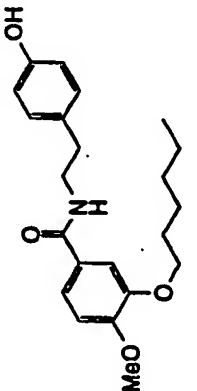
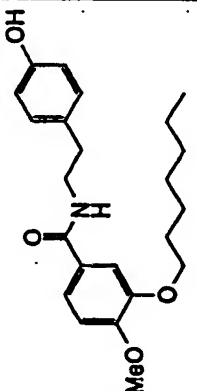
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-7	 <p>Colorless crystals</p>	116~ 117°C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.34(1H, t, J=5.5 Hz) 7.43(1H, dd, J=8.4, 1.8 Hz) 7.40(1H, d, J=1.8 Hz) 7.02(2H, d, J=8.3 Hz) 7.00(1H, d, J=8.2 Hz) 6.67(2H, d, J=8.3 Hz) 3.98(2H, t, J=6.5 Hz) 3.80(3H, s) 3.36(2H, m) 2.70(2H, t, J=7.5 Hz) 1.72(2H, m)	KBr 3310 1613 1549 1514 1272 1238 1135	FAB+ 344 [M ⁺ H] ⁺ (100) 237(27) 223(35) 207(61) 168(60) 153(86)	
2-8	 <p>Colorless crystals</p>	134~ 135°C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.34(1H, t, J=5.5 Hz) 7.41(1H, br d, J=8.4 Hz) 7.39(1H, br s) 7.00(2H, d, J=8.3 Hz) 6.98(1H, d, J=8.2 Hz) 6.66(2H, d, J=8.3 Hz) 3.96(2H, t, J=6.5 Hz) 3.79(3H, s) 3.36(2H, m) 2.69(2H, t, J=7.5 Hz) 1.71(2H, m)	KBr 3445 3256 2940 1641 1556 1509 1323 1267 1224 1188	FAB+ 372 [M ⁺ H] ⁺ (100) 251(30) 235(61)	C ₂₂ H ₂₃ NO ₄ Calcd. C; 71.13% H; 7.87% N; 3.77% Found C; 71.02% H; 7.99% N; 3.74 %
2-9	 <p>Colorless crystals</p>	125~ 126°C	DMSO-d ₆ 300MHz 9.13(1H, s) 8.33(1H, t, J=5.5 Hz) 7.40(1H, dd, J=8.4, 1.9 Hz) 7.37(1H, d, J=1.9 Hz) 7.69(2H, d, J=8.3 Hz) 6.97(1H, d, J=8.2 Hz) 6.65(2H, d, J=8.3 Hz) 3.95(2H, t, J=6.5 Hz) 3.78(3H, s) 3.36(2H, m) 2.68(2H, t, J=7.5 Hz) 1.70(2H, m)	KBr 3452 3263 2921 1642 1615 1549 1510 1442 1318 1269	FAB+ 386 [M ⁺ H] ⁺ (100) 265(15) 249(73) 170(32) 151(40)	C ₂₂ H ₂₃ NO ₄ Calcd. C; 71.66% H; 8.11% N; 3.63% Found C; 71.57% H; 8.24% N; 3.53 %

Table 49

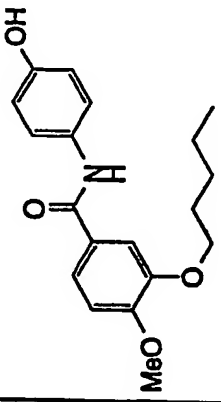
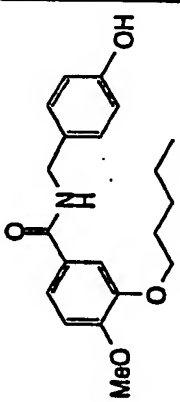
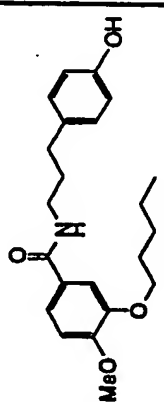
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-10		162.7 ~ 163.2 °C	((CD ₃) ₂ NCDO, 300MHz) 9.80(1H, s) 9.19(1H, s) 7.57(1H, dd, J=8.4, 1.8 Hz) 7.51(1H, d, J=1.8 Hz) 7.48(2H, d, J=8.8 Hz) 7.05(1H, d, J=8.4 Hz) 6.73(2H, d, J=8.8 Hz) 4.02(2H, t, J=6.5 Hz) 3.83(3H, s) 1.7-1.8(2H, m) 1.3-1.5(4H, m) 0.91(3H, t, J=7.9 Hz),	KBr 3295 1642 1514	FAB+ 330 [M ⁺ H] ⁺ (100) 221(70) 154(75)	C ₁₉ H ₂₁ NO ₄ Calcd. C; 69.28% H; 7.04% N; 4.25% Found C; 68.84% H; 7.24% N; 4.25 %
2-11			CDCl ₃ , 300MHz 7.43(1H, d, J=2.1 Hz) 7.26(1H, dd, J=8.3, 2.1 Hz) 7.20(2H, d, J=8.5 Hz) 6.84(1H, d, J=8.3 Hz) 6.81(1H, d, J=8.5 Hz) 6.32(1H, br) 5.80(1H, bs) 4.55(2H, d, J=5.6 Hz) 4.04(2H, t, J=6.9 Hz) 3.89(3H, s) 1.7-1.9(2H, m) 1.3-1.5(4H, m)	KBr 3320 2955 1510	FAB+ 344 [M ⁺ H] ⁺ (100) 238(45) 221(70)	C ₁₉ H ₂₁ NO ₄ Calcd. C; 69.95% H; 7.34% N; 4.08% Found C; 70.05% H; 7.42% N; 4.14 %
2-12			CDCl ₃ , 300MHz 7.37(1H, d, J=2.0 Hz) 7.12(1H, dd, J=8.4, 2.0 Hz) 7.06(2H, d, J=8.4 Hz) 6.83(1H, d, J=8.4 Hz) 6.77(2H, d, J=8.4 Hz) 6.02(1H, br) 5.60(1H, bs) 4.04(2H, t, J=6.9 Hz) 3.89(3H, s) 3.47(2H, q, J=6.2 Hz) 2.65(2H, t, J=6.2 Hz) 1.8-1.9(2H, m)	KBr 3319 2933 1513 1267	FAB+ 372 [M ⁺ H] ⁺ (42) 221(35)	

Table 50

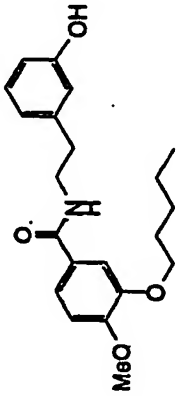
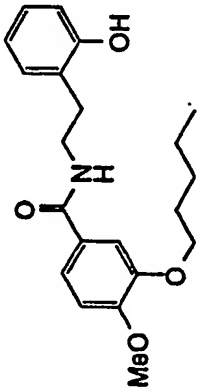
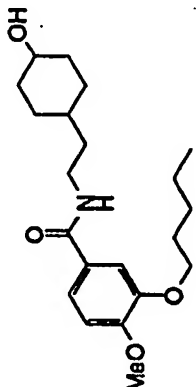
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-13			CDCl ₃ , 300MHz 7.34(1H, d, J=2.0 Hz) 7.17(1H, dd, J=8.3, 2.0 Hz) 7.1-7.2(1H, m) 7.00(1H, bs) 6.80(1H, d, J=8.3 Hz) 6.7-6.8(3H, m) 6.22(1H, bs) 3.99(2H, t, J=6.9 Hz) 3.86(3H, s) 3.55(2H, q, J=6.8 Hz) 2.83(2H, t, J=6.8 Hz) 1.8-1.9(2H, m)	KBr 3319 2954 1581 1505 1268	FAB+ 358 [M ⁺ H] ⁺ (40) 221(50) HRFAB(m/z) Calcd.: C ₂₁ H ₂₄ NO ₄ 358.4622 Found 358.2008	
2-14			CDCl ₃ , 300MHz 7.96(1H, bs) 7.41(1H, d, J=1.9 Hz) 7.26(1H, dd, J=8.3, 1.9 Hz) 7.10(1H, t, J=8.0 Hz) 7.08(2H, d, J=8.0 Hz) 6.92(1H, d, J=8.0 Hz) 6.7-6.9(3H, m) 4.00(2H, t, J=6.8 Hz) 3.86(3H, s) 3.59(2H, q, J=7.0 Hz) 2.96(2H, t, J=7.0 Hz) 1.8-1.9(2H, m)	Neat 3347 2951 1620 1578 1514	FAB+ 358 [M ⁺ H] ⁺ (90) 221(100)	C ₂₁ H ₂₄ NO ₄ Calcd.: C: 70.56% H: 7.61% N: 3.92% Found: C: 70.59% H: 7.77% N: 3.87%
2-15			CDCl ₃ , 300MHz 7.39(1H, d, J=1.9 Hz) 7.21(1H, dd, J=8.3, 1.9 Hz) 6.83(1H, d, J=8.3 Hz) 6.03(1H, bs) 4.04(2H, t, J=6.9 Hz) 3.9-4.0(2H, m) 3.88(3H, s) 3.2-3.6(4H, m) 1.0-2.1(15H, m) 0.91(3H, t, J=7.1 Hz)	Neat 3316 2927 1633 1504 1267	FAB+ 364 [M ⁺ H] ⁺ (50) 221(100) HRFAB(m/z) Calcd.: C ₂₁ H ₂₄ NO ₄ 364.5102 Found 364.2481	

Table 51

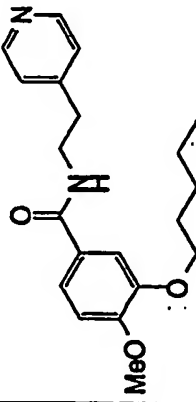
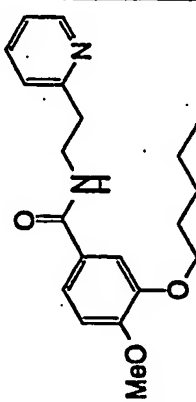
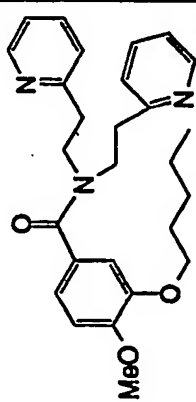
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-16	 <p>Colorless crystals</p>	96~ 98°C	CDCl ₃ , 300MHz 8.52-8.54(2H, m) 7.38(1H, d, J=2.0 Hz) 7.16-7.18(2H, m) 7.15(1H, dd, J=8.5, 2.1 Hz) 6.84(1H, d, J=8.5 Hz) 6.12(1H, br t) 4.05(2H, t, J=7.0 Hz) 3.89(3H, s) 3.72(2H, q, J=7.0 Hz) 2.95(2H, t, J=7.0 Hz) 1.81-1.90(2H, m) 1.35-1.47(4H, m)	Neat 3309 2947 1634 1513 1269	FAB+ 343 [M ⁺ H] ⁺ (100) 285(27) 221(48)	C ₂₀ H ₁₉ N ₃ O ₃ Calcd. C: 70.15% H: 7.65% N: 8.18% Found C: 70.14% H: 7.81% N: 8.12%
2-17	 <p>Colorless crystals</p>	82~ 83°C	CDCl ₃ , 300MHz 8.55-8.57(1H, m) 7.63(1H, td, J=7.6, 1.8 Hz) 7.42(1H, d, J=2.0 Hz) 7.27(1H, dd, J=8.3, 2.0 Hz) 7.15-7.22(2H, m) 6.85(1H, d, J=8.3 Hz) 4.07(2H, t, J=6.9 Hz) 3.90(3H, s) 3.84(2H, q, J=6.0 Hz) 3.10(2H, t, J=6.0 Hz) 1.80-1.90(2H, m) 1.30-1.50(4H, m)	Neat 3242 1630 1508 1272	FAB+ 343 [M ⁺ H] ⁺ (100) 221(52) 154(74)	C ₂₀ H ₁₉ N ₃ O ₃ Calcd. C: 70.15% H: 7.65% N: 8.18% Found C: 70.22% H: 7.86% N: 8.15%
2-18	 <p>Pale-yellow oil</p>		CDCl ₃ , 300MHz 8.38-8.58(2H, m) 7.49-7.64(2H, m) 7.27(1H, d) 7.02-7.19(3H, m) 6.70-6.32(3H, m) 3.95(2H, t, J=6.9 Hz) 3.86(3H, s) 3.55-3.90(4H, m) 2.81-3.33(4H, m) 1.78-1.91(2H, m) 1.30-1.50(4H, m) 0.93(3H, t, J=7.0 Hz)	Neat 2953 1628 1433 1261	FAB+ 448 [M ⁺ H] ⁺ (83) 354(29) 434(33) 221(100)	C ₂₇ H ₂₅ N ₃ O ₃ Calcd. C: 72.46% H: 7.43% N: 9.39% Found C: 71.57% H: 7.66% N: 9.12%

Table 52

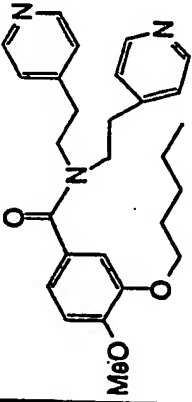
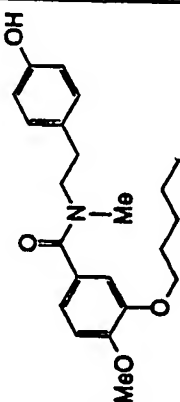
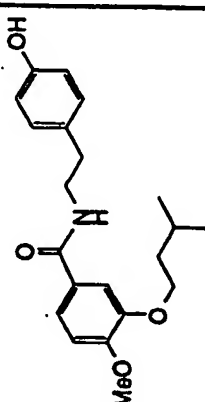
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-19	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 8.50(4H, br s) 7.03(4H, br s) 6.81(1H, d, J=9.0 Hz) 6.66-6.70(2H, m) 3.94(2H, t, J=6.5 Hz) 3.88(3H, s) 3.44-3.73(4H, m) 2.70-3.00(4H, m) 1.79-1.90(2H, m) 1.31-1.50(4H, m) 0.93(3H, t, J=7.3 Hz)	Neat 2933 1628 1601 1261	FAB+ 448 [M+H] ⁺ (55) 390(14) 343(29) 221(100)	
2-20		83.4 ~ 85.2 °C	CDCl ₃ , 300MHz 7.1(1H, bs) 6.8-7.0(6H, m) 6.3(1H, bs) 3.9(2H, d, J=7.5 Hz) 3.9(3H, s) 3.6-3.8(2H, m) 2.6-3.0(2H, m) 2.8(3H, bs) 1.7-1.9(2H, m) 1.3-1.5(4H, m) 0.9(3H, t, J=7.5 Hz)	KBr 3300 2932 2362 1606 1516	FAB+ 372 [M+H] ⁺ (35) 221(40)	C ₂₂ H ₂₃ NO ₄ Calcd. C: 71.13% H: 7.87% N: 3.77% Found C: 71.41% H: 8.07% N: 3.88%
2-21	 <p>Colorless crystals</p>	128 ~ 129 °C	DMSO-d ₆ , 300MHz 9.14(1H, s) 8.34(1H, t) 7.41-7.43(2H, m) 6.97-7.02(3H, m) 6.67(2H, d, J=8.4 Hz) 4.00(2H, t, J=6.8 Hz) 3.79(3H, s) 3.33-3.43(2H, m) 2.70(2H, t, J=7.5 Hz) 1.72-1.86(1H, m) 1.62(2H, q, J=6.8 Hz) 0.91(6H, d, J=6.6 Hz)		FAB+ 358 [M+H] ⁺ (65) 221(99) 150(100)	

Table 53

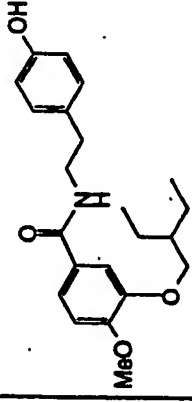
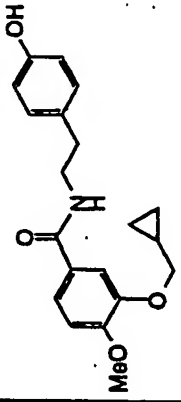
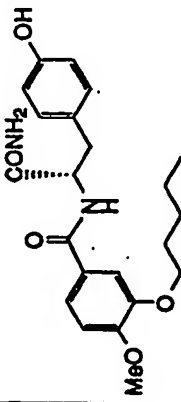
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-22	 <p>Colorless crystals</p>	97~ 98°C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.34(1H, s) 7.41-7.44(2H, m) 6.98-7.03(2H, m) 6.67(2H, d, J=8.4 Hz) 3.86(2H, d, J=5.8 Hz) 3.80(3H, s) 3.27-3.94(2H, m) 2.70(2H, t, J=7.3 Hz) 1.58-1.70(1H, m) 1.33-1.54(4H, m) 0.90(6H, t, J=7.4 Hz)		FAB+ 372 [M ⁺ H] ⁺ (55) 235(71) 150(100)	
2-23	 <p>Colorless crystals</p>	168~ 169°C	DMSO-d ₆ 300MHz 9.14(1H, s) 8.33(1H, t, J=5.4 Hz) 7.37-7.45(2H, m) 6.97-7.02(3H, m) 6.67(2H, d, J=8.3 Hz) 3.80-3.82(5H, m) 3.24-3.44(2H, m) 2.70(2H, t, J=7.4 Hz) 1.13-1.30(1H, m) 0.50-0.63(2H, m) 0.26-0.37(2H, m)		FAB+ 342 [M ⁺ H] ⁺ (100) 205(42) 185(38) 150(50)	
2-24		199.3~ 200.9°C	DMSO-d ₆ 300MHz 9.10(1H, s) 8.22(1H, d, J=8.5 Hz) 7.42(1H, bs) 7.40(1H, d, J=8.48 Hz) 7.35(1H, s) 7.10(2H, d, J=8.41 Hz) 7.01 (2H, bs) 6.78(1H, d, J=8.48 Hz) 6.60(2H, d, J=8.41 Hz) 4.45-4.57(1H, m) 3.92-4.00(2H, m) 3.79(3H, s)	KBr 3600- 3000 1652 1612	FAB+ 401 [M ⁺ H] ⁺ (35) 384(40) 221(100)	C ₂₂ H ₂₂ N ₂ O ₃ Calcd. C: 65.98% H: 7.05% N: 6.99% Found C: 66.02% H: 7.10% N: 6.91%

Table 54

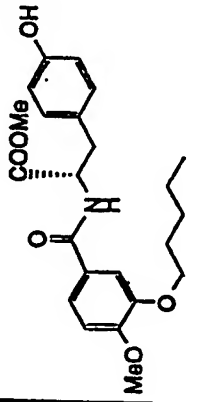
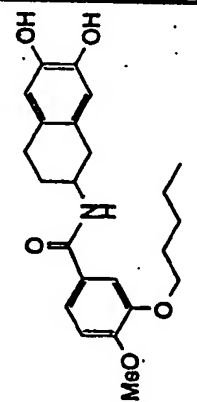
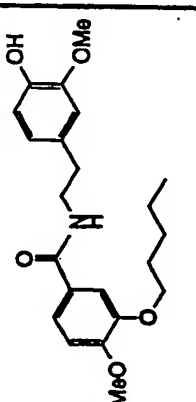
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm} ⁻¹	MS	Elem. anal.
2-25			CDCl ₃ , 300MHz 7.4(1H, d, J=3 Hz) 7.2(1H, dd, J=9.3 Hz) 7.0(2H, d, J=9 Hz) 6.8(1H, d, J=9 Hz) 6.7(2H, d, J=9 Hz) 6.5(1H, m) 5.9(1H, bs) 5.0(1H, m) 4.0(2H, t, J=9 Hz) 3.9(3H, s) 3.8(3H, s) 3.2(2H, m)	Neat 3331 1743 1506	FAB+ 416 [M ⁺ H] ⁺ (30) 237(30) 221(100)	
2-26		160~ 161°C	CDCl ₃ , 300MHz 7.39(1H, d, J=2.0 Hz) 7.21(1H, dd, J=8.1, 2.0 Hz) 6.84(1H, d, J=8.1 Hz) 6.62(1H, s) 6.57 (1H, s) 6.17(1H, d, J=7.7 Hz) 4.29-4.42 (1H, m) 4.04(2H, t, J=7.2 Hz) 3.89(3H, s) 3.05 (1H, dd, J=16.1, 5.2 Hz) 2.75(2H, t, J=6.9 Hz) 2.60(1H, dd, J=16.1, 8.5 Hz)	Neat 3456 1503 1270	FAB+ 400 [M ⁺ H] ⁺ (83) 238(66) 221(100)	C ₂₅ H ₂₉ NO ₃ Calcd. C: 69.15% H: 7.32% N: 3.51% Found C: 68.97% H: 7.39% N: 3.43 %
2-27	 Colorless crystals	152~ 154°C	CDCl ₃ , 300MHz 7.36(1H, d, J=2.0 Hz) 7.13(dd, J=8.3, 2.0 Hz) 6.50-5.91(4H, m) 5.99-6.08(1H, m) 5.52(1H, s) 4.04(2H, t, J=6.9 Hz) 3.89(3H, s) 3.85(3H, s) 3.66(2H, q, J=6.9 Hz) 2.86(2H, t, J=6.9 Hz) 1.80-1.91(2H, m) 1.33-1.50(4H, m)	Neat 3280 1508 1274	FAB+ 388 [M ⁺ H] ⁺ (72) 221(100)	C ₂₄ H ₂₉ NO ₃ Calcd. C: 68.20% H: 7.54% N: 3.61% Found C: 78.23% H: 7.69% N: 3.60 %

Table 55

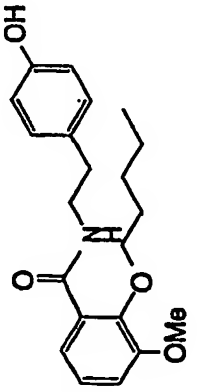
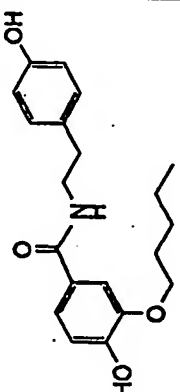
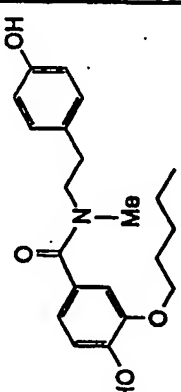
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-28		73.1~ 73.5°C	CDCl ₃ , 300MHz 8.16-8.26(1H, m) 7.70(1H, d, J=8.0 Hz) 7.04-7.16(3H, m) 7.01(1H, d, J=8.0 Hz) 6.79(2H, d, J=8.5 Hz) 6.00(1H, s) 3.85(3H, s) 3.91(2H, t, J=6.9 Hz) 3.85(3H, s) 3.69(2H, q, J=6.68 Hz) 2.85(2H, t, J=7.2 Hz) 1.50-1.65(2H, m)		FAB+ 358 [M ⁺ H] ⁺ (100) 221(40) 150.9(70)	
2-29		76.2~ 77.0°C	DMSO-d ₆ , 300MHz 9.76(1H, d, J=4.4 Hz) 9.13(1H, s) 8.39(1H, d, bs) 7.59(1H, d, J=1.8 Hz) 7.45(1H, d, J=1.8 Hz) 7.36(1H, dd, J=8.8, 1.8 Hz) 6.99(2H, d, J=8.4 Hz) 6.65(2H, d, J=8.4 Hz) 4.02(2H, t, J=6.6 Hz) 3.2-3.4(2H, m) 2.67(2H, t, J=7.5 Hz) 1.7-1.8(2H, m)	KBr 3242 2931 1637 1515 1496		
2-30			DMSO-d ₆ , 300MHz 9.48(1H, bs) 9.20(1H, s) 6.5-7.2(7H, m) 3.9-4.0(2H, m) 3.3-3.5(2H, m) 2.7-3.0(3H, m) 2.6-2.7(2H, m) 1.6-1.8(2H, m) 1.3-1.5(4H, m) 0.87(3H, t, J=7.0 Hz)		FAB+ 358 [M ⁺ H] ⁺ (20)	

Table 56

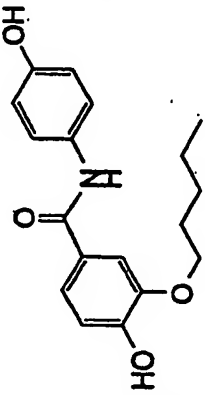
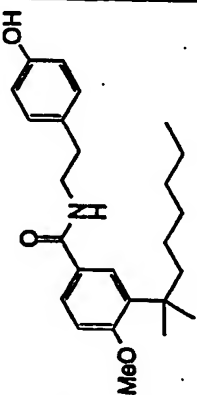
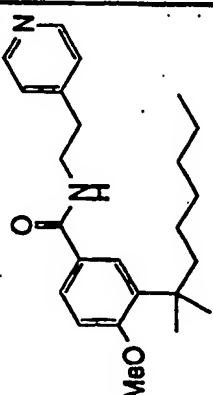
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-31		77.5~ 77.8°C	DMSO-d ₆ , 300MHz 9.84(1H, s) 9.80(1H, d, J=8.1 Hz) 9.22(1H, s) 7.76(1H, dd, J=8.1, 2.0 Hz) 7.49(1H, s) 7.47(2H, d, J=8.8 Hz) 7.42(1H, d, J=8.1 Hz) 6.72(2H, d, J=8.8 Hz) 4.07(2H, t, J=6.6 Hz) 1.7-1.8(2H, m) 1.3-1.4(4H, m) 0.90(3H, t, J=7.2 Hz)	Neat 3383 2955 1646 1602 1513	FAB+ 316 [M+H] ⁺ (25)	
2-32			CDCl ₃ , 300MHz 7.58(1H, s) 7.49(1H, d, J=8.44 Hz) 7.09(2H, d, J=8.36 Hz) 6.81(1H, d, J=8.44 Hz) 6.78(2H, d, J=8.36 Hz) 5.96-6.03(1H, m) 5.18(1H, s) 3.83(3H, s) 3.65(2H, q, J=6.53 Hz) 2.82-2.86 (2H, m) 1.73-1.78(2H, m) 1.32(6H, s)	Neat 3500- 2970 1634	FAB+ 398 [M+H] ⁺ (90) 261(100) 121(42)	
2-33			CDCl ₃ , 300MHz 8.52(2H, d, J=5.99 Hz) 7.60(1H, s) 7.49(1H, d, J=8.49 Hz) 7.17(2H, d, J=5.99 Hz) 6.84(1H, d, J=8.49 Hz) 6.0-6.10(1H, m) 3.85(3H, s) 3.71(2H, q, J=6.66 Hz) 2.95(2H, t, J=6.96 Hz) 1.73-1.83(2H, m) 1.33(6H, s) 1.10-1.27(6H, m)	Neat 3300 1633	FAB+ 383 [M+H] ⁺ (70) 261(60)	

Table 57

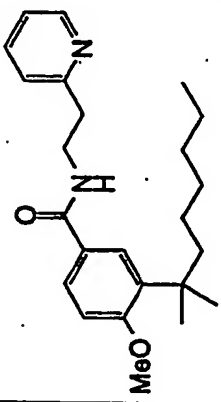
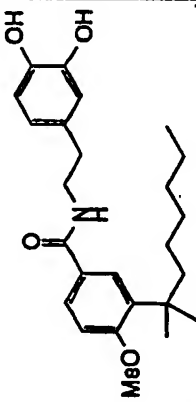
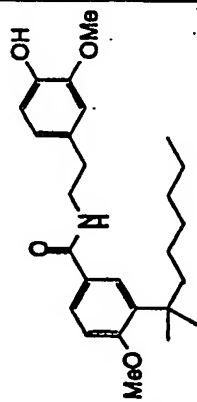
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
2-34			CDCl ₃ , 300MHz 8.56(1H, d, J=4.90 Hz) 7.58-7.68(3H, m) 7.38-7.46(1H, m) 7.14-7.24(2H, m) 6.85(1H, d, J=8.44 Hz) 3.79-3.80(5H, m, involving a singlet at 3.85) 3.10(2H, t, J=6.21 Hz) 1.74-1.82(2H, m) 1.35(6H, s) 1.11-1.24(6H, s) 0.86-0.98(2H, m)	Neat 3316 1634	FAB+ 383 [M ⁺ H] ⁺ (100) 261(70)	
2-35			CDCl ₃ , 300MHz 7.49(1H, bs) 7.58(1H, d, J=2.25 Hz) 7.50(1H, dd, J=8.0, 2.25 Hz) 6.82(2H, d, J=8.18 Hz) 6.76(1H, d, J=1.88 Hz) 6.61(1H, dd, J=8.0, 1.88 Hz) 6.16(1H, d, J=5.56 Hz) 5.95(1H, bs) 3.83(3H, s) 3.61(2H, q, J=6.59 Hz) 2.77(2H, t, J=6.98 Hz) 1.72-1.78(2H, m)	Neat 3600- 3000 1602	FAB+ 414 [M ⁺ H] ⁺ (60) 278(25) 261(100)	C ₂₃ H ₂₇ NO ₄ Calcd. C: 72.01% H: 8.53% N: 3.39% Found C: 72.12% H: 8.92% N: 3.42 %
2-36			CDCl ₃ , 300MHz 7.60(1H, s) 7.47-7.59(1H, m) 6.80-6.89(2H, m) 6.71-6.74(2H, m) 6.00-6.10(1H, m) 5.56(1H, bs) 3.84(3H, s) 3.72(2H, q, J=7.15 Hz) 2.86(2H, t, J=6.7 Hz) 1.73-1.80(2H, m) 1.73-1.80(2H, m) 1.32(6H, s)	KBr 3600- 3050 1625 1602	FAB+ 428 [M ⁺ H] ⁺ (50) 261(100) 150(43)	C ₂₄ H ₂₇ NO ₄ Calcd. C: 73.04% H: 8.72% N: 3.28% Found C: 73.06% H: 8.82% N: 3.27 %

Table 58

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-37		188.9 ~ 189.5 °C	DMSO-d ₆ 300MHz 8.53(2H, bs) 8.15(1H, d, J=7.63 Hz) 7.74(1H, d, J=8.61 Hz) 7.66(1H, s) 7.00(1H, d, J=8.61 Hz) 6.65(1H, s) 6.43(1H, s) 3.95-4.12(1H, m) 3.84(3H, s) 2.59-2.85(4H, m) 1.90-2.03(1H, m) 1.60-1.83(3H, m)	KBr 3282 2416 1599 1531	FAB+ 440 [M ⁺ H] ⁺ (100) 278(60) 261(90)	C ₂₇ H ₂₇ NO ₄ Calcd. C: 73.77% H: 8.48% N: 3.19% Found C: 73.61% H: 8.72% N: 3.22 %
2-38		149.7 ~ 150.2 °C	DMSO-d ₆ 300MHz 9.76(1H, s) 9.13(1H, s) 8.20(1H, t, J=5.49 Hz) 7.58(1H, s) 7.50(1H, d, J=8.36 Hz) 7.01(2H, d, J=8.42 Hz) 6.76(1H, d, J=8.36 Hz) 6.67(2H, d, J=8.42 Hz) 3.27-3.40(5H, m, involving a singlet at 3.06) 2.69(2H, t, J=7.5 Hz) 1.73-1.87(2H, m)	KBr 3450- 3000 1698 1622 1574	FAB+ 384 [M ⁺ H] ⁺ (100) 264(30) 247(60)	C ₂₄ H ₂₃ NO ₃ Calcd. C: 75.16% H: 8.67% N: 3.65% Found C: 74.91% H: 8.85% N: 3.62 %
2-39		159.3 ~ 160.0 °C	DMSO-d ₆ 300MHz 8.77(1H, s) 8.71(1H, s) 8.60(1H, s) 8.17-8.23(1H, m) 7.58(1H, s) 7.48-7.52(1H, m) 6.75 (1H, d, J=8.3 Hz) 6.63(1H, d, J=8.3 Hz) 6.61(1H, s) 6.42-6.47(1H, m) 3.22-3.38(5H, m, involving a singlet at 3.31)	KBr 3700- 3050 1629 1602	FAB+ 400 [M ⁺ H] ⁺ (55) 264(35) 247(100)	C ₂₄ H ₂₃ NO ₄ Calcd. C: 72.15% H: 8.33% N: 3.66% Found C: 71.95% H: 8.56% N: 3.52 %

Table 59

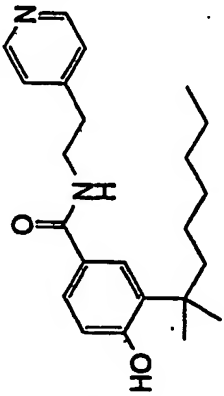
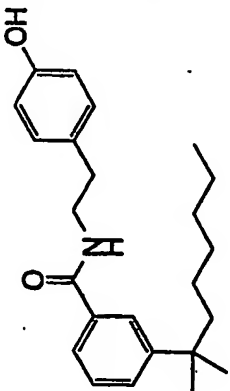
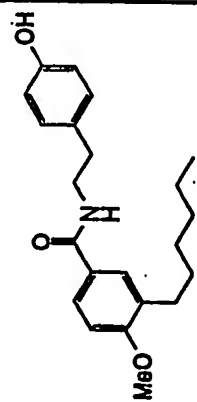
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR _{cm⁻¹}	MS	Elem. anal.
2-40		179.9~ 180.5°C	CDCl ₃ , 300MHz 9.78(1H, s) 8.45(2H, d, J=5.68 Hz) 8.23-8.29(1H, m) 7.56(1H, s) 7.25(2H, d, J=5.68 Hz) 6.75(1H, d, J=8.3 Hz) 3.42-3.51(2H, m) 3.30(3H, s) 2.80-2.88(2H, m) 1.74-1.83(2H, m) 1.30(6H, s) 1.08-1.20(6H, s)	KBr 3450 2950 1632 1602 1575	FAB+ 369 [M ⁺ H] ⁺ (100) 247(20) 169(40)	C ₂₃ H ₂₉ N ₃ O ₂ Calcd. C: 74.96% H: 8.75% N: 7.60% Found C: 74.46% H: 8.90% N: 7.69%
2-41			CDCl ₃ , 300MHz 7.72(1H, s) 7.45(1H, d, J=7.6 Hz) 7.42(2H, d, J=7.6 Hz) 7.31(1H, t, J=7.6 Hz) 7.06(2H, d, J=8.2 Hz) 7.07(1H, s) 7.01(2H, d, J=8.2 Hz) 6.27(1H, t, J=5.5 Hz) 3.67(2H, q, J=6.7 Hz) 2.84(2H, t, J=6.9 Hz) 1.5-1.6(2H, m) 1.28(3H, s)		FAB+ 368 [M ⁺ H] ⁺ (100) 231(80)	
2-42		101.8~ 102.4°C	CDCl ₃ , 300MHz 7.52(1H, d, J=10.3 Hz) 7.49(1H, s) 7.09(2H, d, J=8.46 Hz) 6.81(1H, d, J=10.3 Hz) 6.80(2H, d, J=8.46 Hz) 5.98-6.10(1H, m) 5.32(1H, s) 3.84(3H, s) 3.65(2H, q, J=6.56 Hz) 2.85(2H, t, J=6.92 Hz) 2.59(2H, t, J=7.73 Hz) 1.48-1.60(2H, m)		FAB+ 356.1 [M ⁺ H] ⁺ (100) 236(30) 219(80)	

Table 60

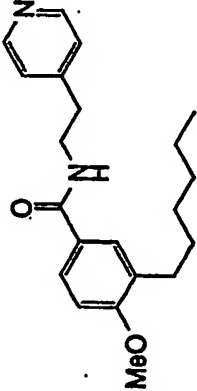
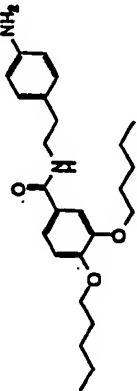
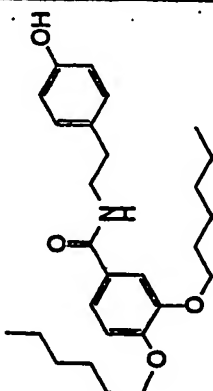
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-43		88.6~ 89.4°C	8.53(1H, d, J=5.97 Hz) 7.52(1H, d, J=8.7 Hz) 7.50(1H, s) 7.18(2H, d, J=5.97 Hz) 6.82(1H, d, J=8.7 Hz) 6.00-6.13(1H, m) 3.85(3H, s) 3.72(2H, q, J=6.67 Hz) 2.95(2H, t, J=6.96 Hz) 2.60(2H, t, J=7.74 Hz) 1.49-1.60(2H, m) 1.25-1.40(4H, m)		FAB+ 341 [M ⁺ H] ⁺ (100) 219(40) 105.9(87)	
2-44		116.6~ 116.9°C	CDCl ₃ , 300MHz 7.34(1H, d, J=2.1 Hz) 7.12(1H, dd, J=8.4, 2.1 Hz) 7.02(2H, d, J=8.3 Hz) 6.83(1H, d, J=8.4 Hz) 6.65(2H, d, J=8.3 Hz) 6.01(1H, br) 4.02(2H, t, J=6.6 Hz) 4.01(2H, t, J=6.6 Hz) 3.63(2H, q, J=6.8 Hz) 3.60(2H, br) 2.80(2H, t, J=6.8 Hz) 1.8-1.9(4H, m)	KBr 3327 2934 1626 1513 1270 1226	FAB+ 413 [M ⁺ H] ⁺ (40) 277(80) 137(100)	C ₁₈ H ₁₈ N ₂ O ₂ Calcd. C: 72.78% H: 8.80% N: 6.79% Found C: 72.91% H: 9.05% N: 6.74%
2-45		127~128°C	CDCl ₃ , 300MHz 7.34 (1H, d, J=2.0 Hz) 7.08-7.26 (3H, m) 6.78-6.83 (3H, m) 6.04 (1H, m) 5.21 (1H, s) 3.99-4.04 (4H, m) 3.65 (2H, q, J=7.0 Hz) 2.85 (2H, t, J=7.0 Hz) 1.77-1.86 (4H, m) 1.31-1.57 (12H, m) 0.88-0.92 (6H, m)		FAB+ 442[M+H] ⁺ (100)	

Table 61

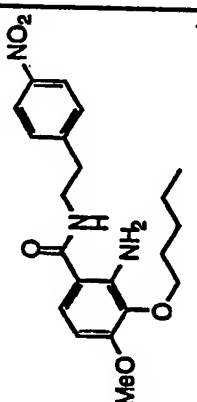
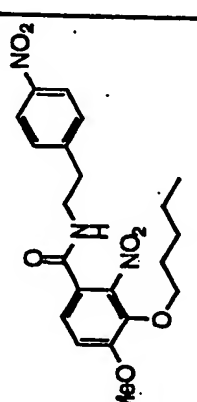
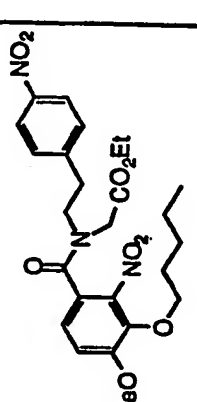
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-46			CDCl ₃ , 300MHz 8.18(2H, d, J=8.4Hz) 7.40(2H, d, J=8.4Hz) 6.91(1H, d, J=8.9Hz) 6.20(1H, d, J=8.9Hz) 5.97(1H, br) 5.78(1H, br) 3.93(2H, t, J=6.7Hz) 3.84(3H, s) 3.69(2H, q, J=6.6Hz) 3.04(2H, t, J=6.9Hz) 1.70-1.83(2H, m) 1.30-1.50(4H, m)			
2-47			CDCl ₃ , 300MHz 8.15(2H, d, J=8.1Hz) 7.39(2H, d, J=8.1Hz) 7.18(1H, d, J=8.7Hz) 6.94(1H, d, J=8.7Hz) 6.11(1H, br) 4.08(2H, t, J=6.6Hz) 3.91(3H, s) 3.64(2H, q, J=6.6Hz) 3.00(2H, t, J=7.1Hz) 1.65-1.77(2H, m) 1.30-1.50(4H, m) 0.94(3H, t, J=7.1Hz)			
2-48			CDCl ₃ , 300MHz 8.19(2H, d, J=8.5Hz) 7.47(2H, d, J=8.5Hz) 7.23(1H, d, J=8.4Hz) 7.00(1H, d, J=8.4Hz) 4.13-4.40(6H, m) 3.92(3H, s) 3.73(2H, br) 3.08(2H, br) 1.70-1.83(2H, m) 1.20-1.45(7H, m) 0.93(3H, t, J=7.0Hz)			

Table 62

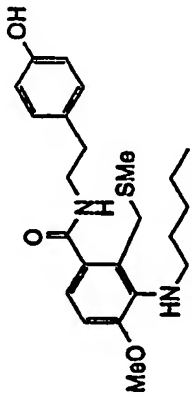
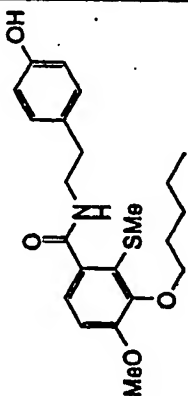
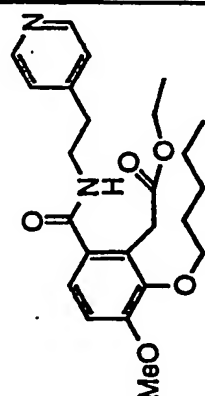
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-49		93.2~ 94.1°C	CDCl ₃ , 300MHz 7.12(2H, d, J=8.5 Hz) 6.98(1H, d, J=8.3 Hz) 6.77(2H, d, J=8.5 Hz) 6.71(1H, d, J=8.3 Hz) 6.35(1H, br) 4.90(1H, br) 3.94(2H, s) 3.83(3H, s) 3.66(2H, q, J=6.6 Hz) 3.11(2H, t, J=7.1 Hz) 2.87(2H, t, J=7.0 Hz) 2.05(3H, s)		FAB+ 417 [M ⁺ H] ⁺ (10) 369(100)	
2-50			CDCl ₃ , 300MHz 7.57(1H, d, J=9.0 Hz) 7.52(1H, br) 7.12(2H, d, J=8.4 Hz) 6.87(1H, d, J=9.0 Hz) 6.78(2H, d, J=8.4 Hz) 5.35(1H, br) 3.96(2H, t, J=6.8 Hz) 3.86(3H, s) 3.71(2H, q, J=6.6 Hz) 2.88(2H, t, J=7.1 Hz) 2.30(3H, s) 1.76-1.90(2H, m)		FAB+ 404 [M ⁺ H] ⁺ (30) 267(100)	
2-51						

Table 63

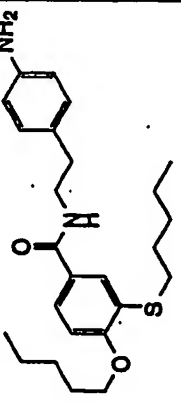
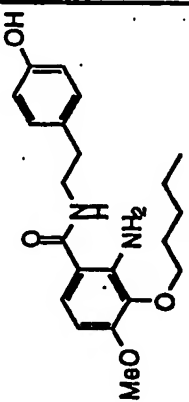
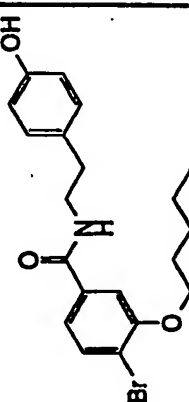
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-52		101.1 ~ 102.6 °C	CDCl ₃ , 300MHz 7.62(1H, d, J=3.0 Hz) 7.40(1H, dd, J=2.1, 8.4 Hz) 7.02(2H, d, J=8.4 Hz) 6.78(1H, d, J=8.4 Hz) 6.66(2H, d, J=8.4 Hz) 5.99(1H, br) 4.04(2H, t, J=6.6 Hz) 3.64(2H, q, J=6.5 Hz) 3.63(2H, br) 2.91(2H, t, J=7.5 Hz) 2.81(2H, t, J=6.8 Hz) 1.7-1.8(2H, m)		FAB+ 429 [M ⁺ H] ⁺ (50) 293(100)	
2-53	 Pale-yellow crystals		CDCl ₃ , 300MHz 7.04(2H, d, J=8.4 Hz) 6.92(1H, d, J=8.7 Hz) 6.78(2H, d, J=8.4 Hz) 6.20(1H, d, J=8.7 Hz) 6.04(1H, br) 5.71(2H, br) 3.92(2H, t, J=6.8 Hz) 3.82(3H, s) 3.59(2H, q, J=6.6 Hz) 2.80(2H, t, J=6.9 Hz) 1.70-1.85(2H, m) 1.30-1.50(4H, m)	0.92(3H, t, J=7.1 Hz)		
2-54	 Colorless crystals	139.8 ~ 140.3 °C	CDCl ₃ , 300MHz 7.53(1H, d, J=8.1 Hz) 7.34(1H, d, J=1.9 Hz) 7.09(2H, d, J=8.5 Hz) 6.96(1H, dd, J=1.9, 8.1 Hz) 6.70(2H, d, J=8.5 Hz) 6.08(1H, br) 5.00(1H, br) 4.06(2H, t, J=6.5 Hz) 3.65(2H, q, J=6.6 Hz) 3.13(2H, t, J=7.1 Hz) 2.85(2H, t, J=6.9 Hz) 1.6-1.75(2H, m)	1.33-1.5(4H, m) 0.92(3H, t, J=7.2 Hz)	FAB+ 407 [M ⁺ H] ⁺ (20) 271(20)	

Table 64

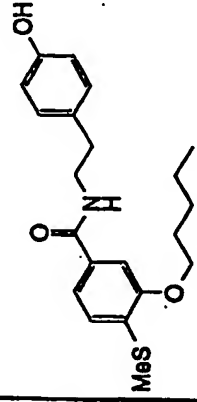
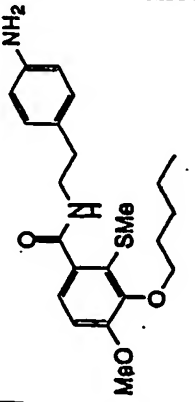
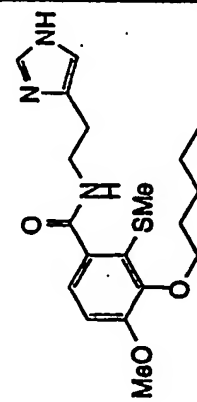
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-55	 <p>Colorless crystals</p>	148.2~ 149.3 °C	CDCl ₃ , 300MHz 7.27(1H, d, J=1.5 Hz) 7.04-7.13(4H, m) 6.80(2H, d, J=8.4 Hz) 6.06(1H, br) 4.95(1H, s) 4.07(2H, t, J=6.5 Hz) 3.67(2H, q, J=6.5 Hz) 2.86(2H, t, J=7.7 Hz) 2.43(3H, s) 1.78-1.92(2H, m) 1.37-1.5(4H, m) 0.94(3H, t, J=7.1 Hz)		FAB+ 374 [M ⁺ H] ⁺ (30) 307(20)	
2-56	 <p>Pale-yellow crystals</p>	80.8~ 82.7 °C	CDCl ₃ , 300MHz 7.53(1H, d, J=8.7 Hz) 7.35(1H, br) 7.02(2H, d, J=8.3 Hz) 6.87(1H, d, J=8.7 Hz) 6.63(2H, d, J=8.3 Hz) 3.95(2H, t, J=6.7 Hz) 3.85(3H, s) 3.69(2H, q, J=5.7 Hz) 3.57(2H, br) 2.83(2H, t, J=6.9 Hz) 2.31(3H, s) 1.75-1.88(2H, m)		FAB+ 403 [M ⁺ H] ⁺ (50) 267(100)	
2-57	 <p>Colorless crystals</p>	98.6~ 99.3 °C	CDCl ₃ , 300MHz 7.62(1H, br) 7.56(1H, s) 7.48(1H, d, J=8.7 Hz) 6.87(1H, d, J=8.7 Hz) 6.87(1H, s) 3.97(2H, t, J=6.6 Hz) 3.86(3H, s) 3.78(2H, q, J=6.3 Hz) 2.97(2H, t, J=6.5 Hz) 2.36(3H, s) 1.75-1.88(2H, m) 1.3-1.55(4H, m)		FAB+ 378 [M ⁺ H] ⁺ (100) 267(50)	

Table 65

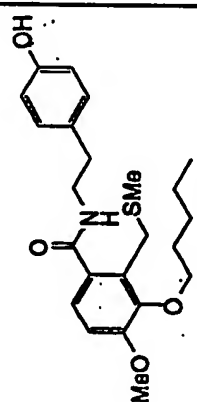
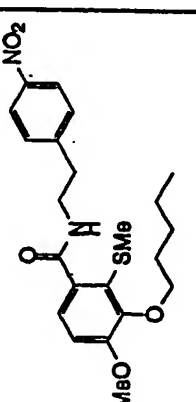
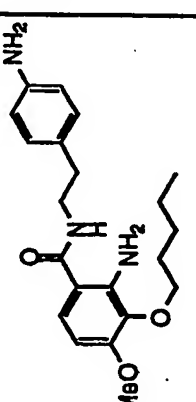
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-58			CDCl ₃ , 300MHz 7.20(1H, d, J=5 Hz) 7.12(2H, d, J=8.6 Hz) 6.79(1H, d, J=8.5 Hz) 6.78(2H, d, J=8.6 Hz) 6.70(1H, bs) 5.06(1H, s) 3.95(2H, t, J=6.7 Hz) 3.91(2H, s) 3.85(3H, s) 3.67(2H, q, J=6.6 Hz) 2.88(2H, t, J=7.0 Hz) 1.75-1.87(2H, m)		FAB+ 418 [M+H] ⁺ (30) 281(100)	
2-59	 Colorless crystals	99.3 ~ 100.1 °C	CDCl ₃ , 300MHz 8.18(2H, d, J=8.7 Hz) 7.63(1H, bs) 7.60(1H, d, J=8.6 Hz) 7.45(2H, d, J=8.7 Hz) 6.90(1H, d, J=8.6 Hz) 3.96(2H, t, J=6.7 Hz) 3.87(3H, s) 3.78(2H, q, J=6.6 Hz) 3.09(2H, t, J=7.0 Hz) 2.39(3H, s) 1.75-1.92(H, m) 1.32-1.54(4H, m)		FAB+ 433 [M+H] ⁺ (40) 267(100)	
2-60	 Colorless crystals	97.4 ~ 98.3 °C	CDCl ₃ , 300MHz 7.02(2H, d, J=7.8 Hz) 6.91(1H, d, J=8.7 Hz) 6.66(2H, d, J=7.8 Hz) 6.19(1H, d, J=8.7 Hz) 5.92(1H, bs) 5.77(2H, bs) 3.92(2H, t, J=6.8 Hz) 3.83(3H, s) 3.61(2H, bs) 3.60(2H, q, J=6.5 Hz) 2.79(2H, t, J=6.9 Hz) 1.7-1.93(2H, m)	KBr 3455 3311 2936 1621 1535 1287	FAB+ 372 [M+H] ⁺ (20) 236(50)	C ₂₁ H ₂₉ N ₃ O ₃

Table 66

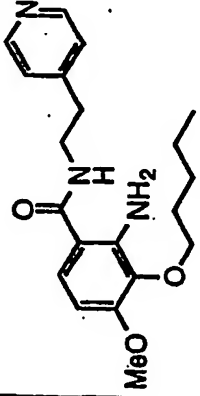
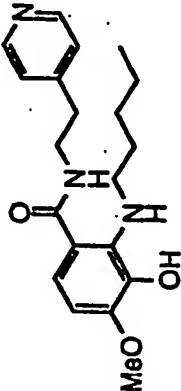
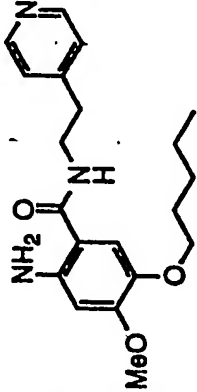
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-61	 <p>Colorless crystals</p>	86.5~ 87.6°C	CDCl ₃ 300MHz 8.53(2H,d,J=6.0Hz) 7.16(2H,d,J=6.0Hz) 6.91(1H,d,J=8.9Hz) 6.19(1H,d,J=8.9Hz) 5.96(1H,b) 5.78(1H,b) 3.92(2H,t,J=6.8Hz) 3.83(3H,s) 3.66(2H,q,J=6.6Hz) 2.91(2H,t,J=6.9Hz) 1.70-1.83(2H,m) 1.30-1.50(4H,m)	KBr 3345 1626 1530 1282	FAB+ 358 [M+H] ⁺ (60) 236(70)	C ₂₀ H ₂₇ N ₃ O ₃
2-62	 <p>Pale-orange crystals</p>	116.8~ 117.6°C	CDCl ₃ 300MHz 8.77(1H,b) 8.52(2H,d,J=6.1Hz) 7.50(1H,d,J=8.8Hz) 7.23(2H,d,J=6.1Hz) 6.64(1H,d,J=8.8Hz) 3.91(3H,s) 3.73(2H,q,J=6.2Hz) 2.96(2H,t,J=7.1Hz) 2.87(2H,t,J=7.2Hz) 1.40-1.58(2H,m) 1.20-1.40(4H,m) 0.98(3H,t,J=6.8Hz)	KBr 3330 2955 1630 1529 1289	FAB+ 358 [M+H] ⁺ (50) 307(20)	C ₂₀ H ₂₇ N ₃ O ₃
2-63	 <p>Colorless crystals</p>	128.7~ 129.4°C	CDCl ₃ 300MHz 8.53(2H,d,J=6.0Hz) 7.18(2H,d,J=6.0Hz) 6.73(1H,s) 6.18(1H,s) 5.99(1H,b) 5.35(2H,b) 3.85(2H,t,J=6.6Hz) 3.83(3H,s) 3.67(2H,q,J=6.7Hz) 2.93(2H,t,J=7.1Hz) 1.70-1.80(2H,m) 1.30-1.50(4H,m)	KBr 3332 2930 1632 1598 1542 1259 1214	FAB+ 358 [M+H] ⁺ (40) 236(100)	C ₂₀ H ₂₇ N ₃ O ₃

Table 67

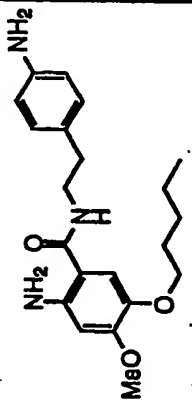
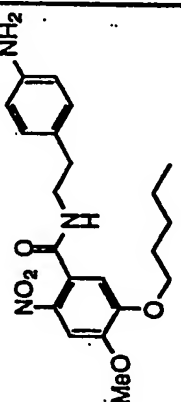
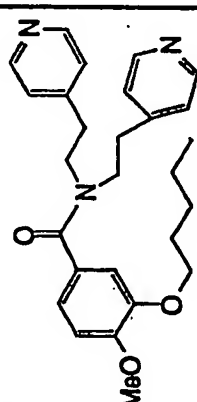
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-64	 <p>Orange crystals</p>	125.7~ 127.2°C	CDCl ₃ , 300MHz 7.59(1H, s) 7.03(2H, d, J=8.4Hz) 6.77(1H, s) 6.63(2H, d, J=8.4Hz) 5.64(1H, br) 4.05(2H, t, J=6.8Hz) 3.93(3H, s) 3.68(2H, q, J=6.5Hz) 3.60(2H, br s) 2.85(2H, t, J=6.8Hz) 1.80-1.90(2H, m) 1.30-1.45(4H, m)	KBr 3258 2934 1650 1514 1336 1272 1220	FAB+ 402 [M+H] ⁺ (20) 266(20)	C ₂₁ H ₂₉ N ₃ O ₃
2-65	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 7.59(1H, s) 7.03(2H, d, J=8.4Hz) 6.77(1H, s) 6.63(2H, d, J=8.4Hz) 5.64(1H, br) 4.05(2H, t, J=6.8Hz) 3.93(3H, s) 3.68(2H, q, J=6.5Hz) 3.60(2H, br s) 2.85(2H, t, J=6.8Hz) 1.80-1.90(2H, m) 1.30-1.45(4H, m)	Neat 3258 2934 1650 1514 1336 1272 1221	FAB+ 402 [M+H] ⁺ (20) 266(20)	C ₂₁ H ₂₇ N ₃ O ₃
2-66	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 8.50(4H, br s) 7.03(4H, br s) 6.81(1H, d, J=9.0 Hz) 6.66-6.70(2H, m) 3.94(2H, t, J=6.5 Hz) 3.88(3H, s) 3.44-3.73(4H, m) 2.70-3.00(4H, m) 1.79-1.90(2H, m) 1.31-1.50(4H, m) 0.93(3H, t, J=7.3 Hz)	Neat 2933 1628 1601 1261	FAB+ 448 [M+H] ⁺ (55) 390(14) 343(29) 221(100)	

Table 68

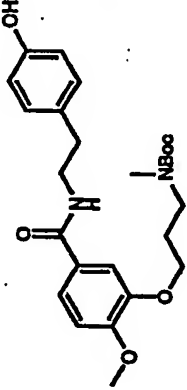
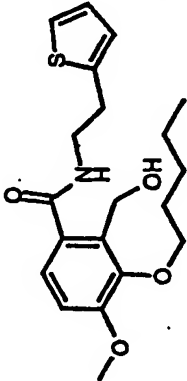
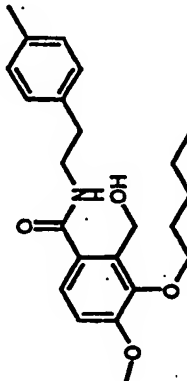
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-67	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 7.1-7.5 (3H, m) 7.08 (2H, d, J = 8.4 Hz) 6.86 (2H, d, J = 8.4 Hz) 6.80 (1H, bs) 5.91 (1H, bs) 3.99 (2H, bs) 3.87 (3H, s) 3.64 (2H, q, J = 6.3 Hz) 3.42 (2H, t, J = 6.6 Hz) 2.87 (3H, s) 2.84 (2H, t, J = 6.6 Hz) 2.0-2.1 (2H, m)		FAB+ 459 [M+H+](50)	
2-68	 <p>Pale-yellow crystals</p>		CDCl ₃ , 300MHz 7.18 (1H, d, J = 4.8 Hz) 7.18 (1H, d, J = 8.4 Hz) 6.96 (1H, dd, J = 4.8, 3.3 Hz) 6.88 (1H, d, J = 3.3 Hz) 6.81 (1H, d, J = 8.4 Hz) 6.35 (1H, bs) 4.67 (2H, d, J = 6.9 Hz) 4.14 (1H, t, J = 6.9 Hz) 3.97 (2H, t, J = 6.6 Hz) 3.86 (3H, s) 3.72 (2H, q, J = 6.3 Hz) 3.16 (2H, t, J = 6.3 Hz)		FAB+ 378 [M+H+](30), 360(100)	
2-69	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.11 (4H, s) 7.10 (1H, d, J = 8.4 Hz), 6.78 (1H, d, J = 8.4 Hz), 6.20 (1H, bs) 4.63 (2H, d, J = 6.9 Hz), 4.20 (1H, t, J = 6.6 Hz), 3.96 (2H, t, J = 6.6 Hz), 3.84 (3H, s), 3.07 (2H, q, J = 6.6 Hz) 2.88 (2H, t, J = 6.6 Hz) 2.32 (3H, s) 1.7-1.9 (4H, m)		FAB+ 386 [M+H+](30) 368(100)	

Table 69

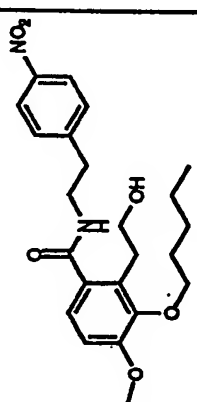
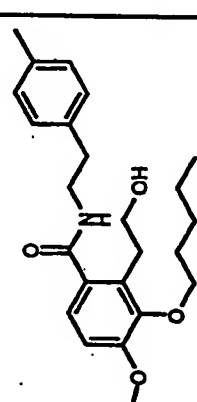
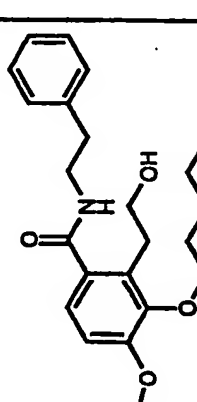
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm} ⁻¹	MS	Elem. anal.
2-70	 <p>Pale-yellow solid</p>		CDCl ₃ 300MHz 8.18(2H, d, J=8.4 Hz), 7.42(2H, d, J=8.4 Hz), 7.09(1H, d, J=8.4 Hz), 6.78(1H, d, J=8.4 Hz), 6.75(1H, bs) 3.94(2H, t, J=6.9 Hz) 3.90(2H, q, J=5.4 Hz) 3.85(3H, s) 3.72(2H, q, J=6.9 Hz) 3.60(1H, t, J=4.8 Hz) 3.06(2H, t, J=6.9 Hz) 2.92(2H, t, J=5.7 Hz),		FAB+ 431[M+H+] (100), 413 (80).	
2-71	 <p>Colorless crystals</p>		CDCl ₃ 300MHz 7.13(4H, s) 7.05(1H, d, J=8.4 Hz), 6.75(1H, d, J=8.4 Hz), 6.36(1H, bs) 4.03(1H, t, J=4.8 Hz) 3.94(2H, t, J=6.9 Hz) 3.87(2H, t, J=5.4 Hz) 3.84(3H, s) 3.67(2H, q, J=6.6 Hz) 2.94(2H, q, J=5.4 Hz) 2.88(2H, t, J=5.4 Hz) 2.33(3H, s)		FAB+ 400[M+H+] (100), 382 (30).	
2-72	 <p>Colorless crystals</p>		CDCl ₃ 300MHz 7.2-7.4(5H, m) 7.04(1H, d, J=8.4 Hz), 6.75(1H, d, J=8.4 Hz), 6.46(1H, bs) 3.98(1H, t, J=5.0 Hz) 3.94(2H, t, J=6.6 Hz) 3.86(2H, t, J=5.1 Hz) 3.83(3H, s) 3.69(2H, q, J=6.6 Hz) 2.9-3.0(4H, m) 1.75(2H, t, J=7.1 Hz) 1.3-1.5(4H, m)		FAB+ 386[M+H+] (100)	

Table 70

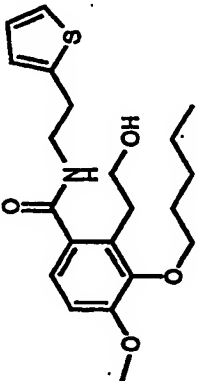
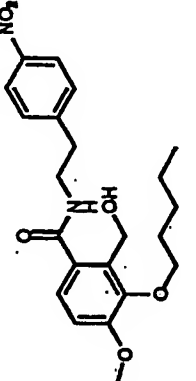
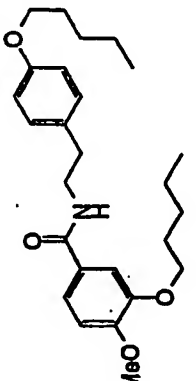
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm} ⁻¹	MS	Elen. anal.
2-73	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.16(1H, dd, J=4.7, 1.0 Hz) 7.10(1H, d, J=8.5 Hz), 6.95(1H, dd, J=4.7, 3.3 Hz), 6.87(1H, dd, J=3.3, 1.0 Hz) 6.73(1H, d, J=8.5 Hz) 6.62(1H, bs) 3.94(2H, t, J=6.6 Hz) 3.9-4.0(3H, m) 3.84(3H, s)		FAB+ 392[M+H+] (100), 374(25)	
2-74	 <p>Yellow crystals</p>		CDCl ₃ , 300MHz 8.18(2H, d, J=8.7 Hz) 7.41(2H, d, J=8.7 Hz) 7.16(1H, d, J=8.4 Hz) 6.82(1H, d, J=8.4 Hz) 6.40(1H, bs) 4.65(2H, t, J=6.6 Hz), 3.97(2H, t, J=6.6 Hz), 3.92(1H, t, J=6.6 Hz), 3.86(3H, s) 3.74(2H, q, J=6.6 Hz) 3.07(2H, t, J=6.6 Hz) 1.7-1.9(2H, m)		FAB+ 417 [M+H+](20), 399(100)	
2-75						

Table 71

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-76			CDCl ₃ , 300MHz 7.28 (1H, s) 7.23 (1H, t, J=8.0 Hz) 7.15 (1H, d, J=8.0 Hz) 7.08 (1H, s) 7.02 (2H, d, J=8.4 Hz) 6.98 (1H, d, J=8.0 Hz) 6.83 (2H, d, J=8.4 Hz) 6.32 (1H, br) 3.93 (2H, t, J=7.6 Hz) 3.64 (2H, q, J=7.0 Hz) 2.81 (2H, t, J=7.0 Hz) 1.7-1.8 (2H, m)	NaCl 3314 2932 1638 1580 1515	FAB+ 328[M+H+] (100) 191(75)	
2-77		113.5~ 114.2°C	CDCl ₃ , 300MHz 7.43 (1H, d, J=2.0 Hz) 7.26 (2H, dd, J=8.4, 2.0 Hz) 6.85 (1H, d, J=8.4 Hz) 6.76 (1H, br) 4.06 (2H, t, J=6.9 Hz) 3.90 (3H, s) 3.73 (4H, t, J=4.6 Hz) 3.55 (2H, q, J=5.7 Hz) 2.62 (2H, t, J=5.7 Hz) 2.53 (4H, t, J=4.6 Hz) 1.8-1.9 (2H, m)	KBr 3286 2945 1654 1617 1515	FAB+ 351[M+H+] (100) 221(80) 264(60)	C ₁₉ H ₃₀ N ₂ O ₄ Calcd. C: 65.12% H: 8.63% N: 7.99% Found C: 65.02% H: 8.56% N: 8.30%
2-78						

Table 72

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-79			CDC13-300MHz 7.4-7.7 (5H, m) 7.2-7.4 (1H, m) 6.6-6.9 (7H, m) 3.92 (2H, t, J=6.8 Hz) 3.87 (3H, s) 3.6-4.0 (2H, m) 3.5-3.7 (2H, m) 3.3-3.5 (1H, m) 3.0-3.2 (1H, m) 2.6-2.8 (2H, m) 1.7-1.9 (2H, m) 1.3-1.5 (4H, m)	Neat 3234 1609 1516	FAB+ 510 [M+H] ⁺ (65) 384(45) 221(100)	
2-80		89.2~ 90.4°C	CDC13-300MHz 7.3 (1H, d, J=3 Hz) 7.2 (1H, dd, J=9, 3 Hz) 7.0 (2H, d, J=9 Hz) 6.8 (1H, d, J=9 Hz) 6.6 (1H, bs) 6.4 (1H, bt) 4.3-4.4 (1H, m) 4.0 (2H, t, J=7.5 Hz) 3.9 (3H, s) 3.4-3.8 (2H, m) 3.2 (1H, m) 2.8-2.9 (2H, m)	KBr 3324 2954 1616 1515 1264	FAB+ 388 [M+H] ⁺ (45) 221(100)	C ₂₂ H ₂₉ NO ₅ Calcd. C: 68.20% H: 7.54% N: 3.61% Found C: 67.74% H: 7.72% N: 3.62%
2-81			DMSO-d6-300MHz 12.50 (1H, bs) 9.14 (1H, s) 8.43 (1H, d, J=8.2 Hz) 7.42 (2H, bd, J=8.5 Hz) 7.35 (1H, bs) 7.10 (2H, d, J=8.3 Hz) 7.00 (1H, d, J=8.5 Hz) 6.63 (2H, d, J=8.3 Hz) 4.4-4.6 (1H, m) 3.97 (2H, t, J=6.4 Hz) 3.80 (3H, s) 2.9-3.0 (2H, m)	KBr 3431 3303 1740 1641 1509	FAB+ 402 [M+H] ⁺ (60) 221(100) 237(42)	C ₂₂ H ₂₇ NO ₆ Calcd. C: 65.82% H: 6.78% N: 3.49% Found C: 63.00% H: 6.84% N: 3.26%

Table 73

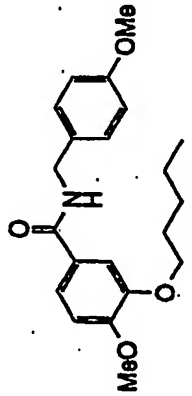
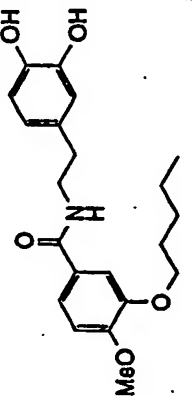
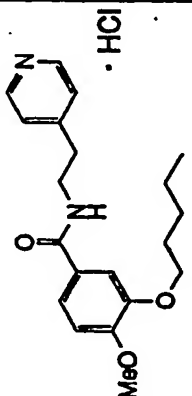
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR, cm ⁻¹	MS	Elem. anal.
2-82						
2-83	 Colorless crystals		DMSO-d ₆ 300MHz 8.55-8.80 (2H, m) 8.35 (1H, t) 7.38-7.47 (2H, m) 7.00 (1H, d, J=8.5 Hz) 6.64 (1H, d, J=8.5 Hz) 6.62 (1H, d, J=2.2 Hz) 6.46 (1H, dd, J=8.5, 2.2 Hz) 3.98 (2H, t, J=6.7 Hz) 3.80 (3H, s) 3.29-3.41 (2H, m) 2.63 (2H, t, J=8.3 Hz)	3435 3253 1561 1508 1275	FAB+ 374 [M+H] ⁺ (37) 307(19) 238(45) 169(57) 154(100)	C ₂₁ H ₂₇ NO ₅ Calcd. C: 67.54% H: 7.29% N: 3.75% Found C: 68.30% H: 7.49% N: 3.65%
2-84	 Pale-yellow amorphous		DMSO-d ₆ 300MHz 8.74 (2H, d, J=6.0 Hz) 8.50 (1H, brs) 7.81 (2H, d, J=6.0 Hz) 7.38-7.42 (2H, m) 6.99 (1H, d, J=8.0 Hz) 3.96 (2H, t, J=6.8 Hz) 3.80 (3H, s) 3.60 (2H, q, J=6.5 Hz) 3.10 (2H, t, J=6.5 Hz) 1.66-1.78 (2H, m) 1.27-1.46 (4H, m) 0.90 (3H, t, J=6.5 Hz)	2934 1638 1505 1268	FAB+ 343 [M+H-HCl] ⁺ (100)	

Table 74

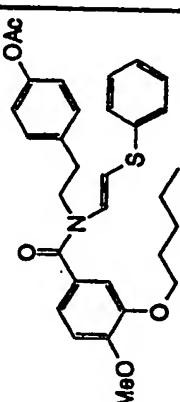
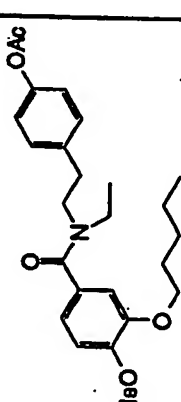
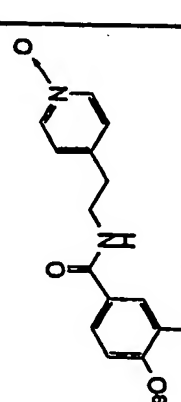
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-85			CDCl ₃ 300MHz 7.1-7.3 (5H, m) 7.27 (1H, d, J=8.2 Hz) 7.22 (2H, d, J=8.5 Hz) 7.04 (2H, d, J=8.5 Hz) 6.9-7.1 (2H, m) 6.87 (1H, d, J=8.2 Hz) 5.68 (1H, d, J=13.6 Hz) 4.11 (2H, t, J=7.8 Hz) 3.98 (2H, t, J=6.9 Hz) 3.90 (3H, s) 3.03 (2H, t, J=7.8 Hz) 2.29 (3H, s)	Neat 2932 1760 1659 1600		
2-86			CDCl ₃ 300MHz 6.8-7.3 (7H, m) 3.99 (2H, t, J=6.9 Hz) 3.88 (3H, s) 3.2-3.8 (4H, m) 2.8-3.0 (2H, m) 2.28 (3H, s) 1.8-1.9 (2H, m) 1.3-1.5 (4H, m) 1.0-1.2 (3H, m) 0.92 (3H, t, J=7.1 Hz)	Neat 2933 1762 1628	FAB+ 428 [M+H+] ⁺ (25) 221(100)	
2-87	 Colorless oil		CDCl ₃ 300MHz 8.07 (2H, brd) 7.41 (1H, d, J=1.7 Hz) 7.20 (1H, brd, J=8.3 Hz) 7.13 (2H, d, J=6.5 Hz) 6.84 (1H, d, J=8.3 Hz) 6.44-6.65 (1H, m) 4.05 (2H, t, J=6.9 Hz) 3.90 (3H, s) 3.69 (2H, q, J=6.7 Hz) 2.96 (2H, t, J=6.7 Hz) 1.78-1.90 (2H, m) 1.30-1.50 (4H, m)		FAB+ 359 [M+H+] ⁺ (95) 221(55) 151(53) 122(100)	

Table 75

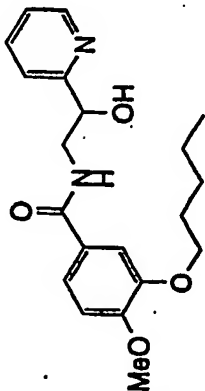
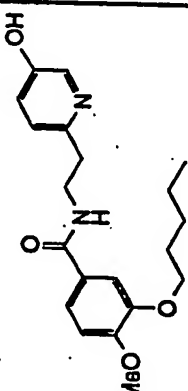
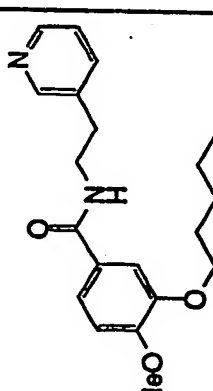
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-88	 <p>Colorless crystals</p>	110~112 °C	CDCl ₃ 300MHz 8.54-8.56 (1H, m) 7.73 (1H, td, J=7.7, 1.9 Hz) 7.48 (1H, d, J=7.9 Hz) 7.36 (1H, d, J=1.9 Hz) 7.22-7.27 (2H, m) 6.35 (1H, d, J=8.4 Hz) 5.00 (2H, m) 3.99-4.09 (3H, m) 3.90 (3H, s) 3.60-3.69 (1H, m)	3310 1637 1510 1269 1230	FAB+ 359 [M+H] ⁺ (51) 307 (27) 221 (36) 154 (100)	C ₂₀ H ₂₆ N ₂ O ₄ Calcd. C: 67.02% H: 7.31% N: 7.82% Found C: 67.11% H: 7.43% N: 7.78%
2-89	 <p>Colorless crystals</p>	117~118 °C	CDCl ₃ 300MHz 8.18 (1H, d, J=2.9 Hz) 7.39 (1H, d, J=1.8 Hz) 7.05 (1H, dd, J=8.3, 1.8 Hz) 7.17-7.25 (1H, m) 7.14 (1H, dd, J=8.2, 2.9 Hz) 7.08 (1H, d, J=8.2 Hz) 6.85 (1H, d, J=8.3 Hz) 4.04 (2H, t, J=6.7 Hz) 3.89 (3H, s) 3.79 (2H, q, J=6.4 Hz)		FAB+ 359 [M+H] ⁺ (35) 221 (29) 154 (100)	
2-90	 <p>Colorless crystals</p>	93~94 °C	CDCl ₃ 300MHz 8.46-8.52 (2H, m) 7.54-7.60 (1H, m) 7.36 (1H, d, J=2.0 Hz) 7.22-7.28 (1H, m) 7.14 (1H, dd, J=8.3, 2.0 Hz) 6.82 (1H, d, J=8.3 Hz) 6.00-6.11 (1H, m) 4.04 (2H, t, J=6.9 Hz) 3.88 (3H, s) 3.69 (2H, q, J=6.8 Hz) 2.95 (2H, t, J=6.8 Hz)	3316 1521 1272 1231		C ₂₀ H ₂₆ N ₂ O ₃ Calcd. C: 70.15% H: 7.65% N: 8.18% Found C: 70.18% H: 7.85% N: 8.12%

Table 76

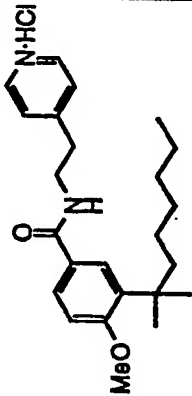
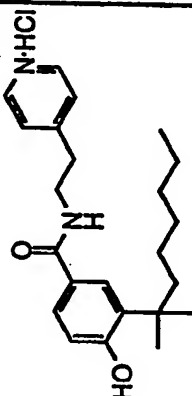
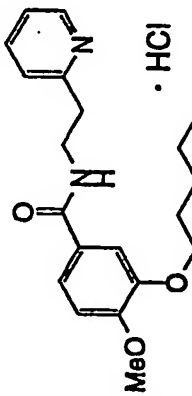
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-91	 <p>Colorless crystals</p>		DMSO-d ₆ 300MHz 8.83(2H,d,J=6.4Hz) 8.47(1H,bs) 7.98(2H,d,J=6.4Hz) 7.65(1H,d,J=8.5Hz) 7.59(1H,s) 6.98(1H,d,J=8.5Hz) 5.05(1H,bs) 3.82(3H,s) 3.62(2H,q,J=6.0Hz) 3.16(2H,t,J=6.5Hz) 1.70-1.80(2H,m) 1.29(6H,s)		FAB- 418 [M-H+](20) 417(100) 381(90)	C ₂₄ H ₃₅ N ₂ O ₂ Cl
2-92	 <p>Colorless crystals</p>		DMSO-d ₆ 300MHz 9.85(1H,s) 8.77(2H,d,J=6.4Hz) 8.30(1H,bs) 7.87(2H,d,J=6.4Hz) 7.54(1H,s) 7.45(1H,d,J=8.3Hz) 6.76(1H,d,J=8.3Hz) 3.53-3.63(2H,m) 3.03-3.14(2H,m) 1.72-1.82(2H,m) 1.27(6H,s) 1.10-1.25(6H,m)		FAB- 403 [M-H+](10) 367(100)	C ₂₃ H ₃₃ N ₂ O ₂
2-93	 <p>• HCl</p>					

Table 77

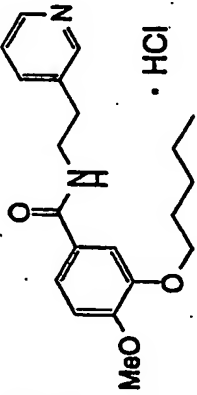
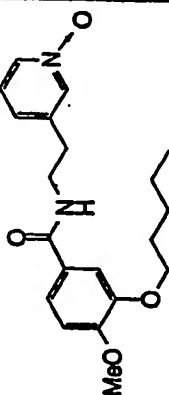
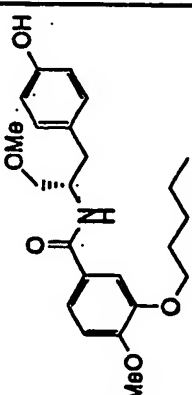
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-94						
2-95	 Pale-purple crystals	104~106 °C	CDCl ₃ 300MHz 8.03-8.11 (2H, m) 7.40 (1H, d, J=2.0 Hz) 7.16-7.26 (3H, m) 6.82 (1H, d, J=8.4 Hz) 6.58-6.70 (1H, m) 4.04 (2H, t, J=6.9 Hz) 3.89 (3H, s) 3.67 (2H, q, J=6.8 Hz) 2.92 (2H, t, J=6.8 Hz) 1.71-1.90 (2H, m) 1.30-1.50 (4H, m) 0.92 (3H, t, J=7.0 Hz)	3318 1631 1512 1265	FAB+ 359[M+H+] (100) 301(16) 221(21)	
2-96			CDCl ₃ 300MHz 7.37 (1H, d, J=2.0 Hz) 7.22 (1H, dd, J=8.4, 2.0 Hz) 7.07 (2H, d, J=8.3 Hz) 7.01 (1H, bs) 6.83 (2H, d, J=8.4 Hz) 6.78 (1H, d, J=8.3 Hz) 6.47 (1H, bs) 4.3-4.5 (1H, m) 4.02 (2H, t, J=6.9 Hz) 3.88 (3H, s) 3.41 (2H, d, J=3.6 Hz)	3300 2933 1632 1504 1266	FAB+ 402 [M+H+](60) 221(80)	C ₂₃ H ₂₂ NO ₅

Table 78

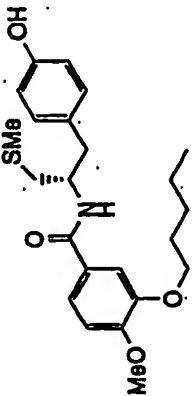
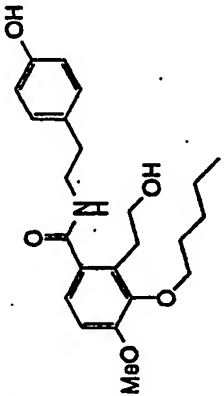
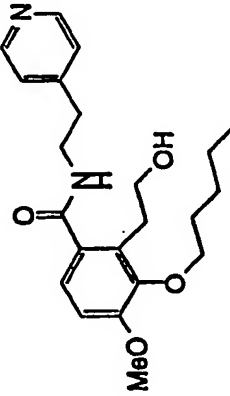
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-97			CDCl ₃ , 300 MHz 7.36 (1H, d, J=2.0 Hz) 7.18 (1H, dd, J=8.3, 2.0 Hz) 7.09 (2H, d, J=8.3 Hz) 6.84 (1H, d, J=8.3 Hz) 6.77 (2H, d, J=8.3 Hz) 6.23 (1H, bd, J=6.9 Hz) 6.0 (1H, bs) 4.4-4.6 (1H, m) 4.00 (2H, t, J=6.8 Hz) 3.89 (3H, s)	Neat 3500 2926 1631 1512 1267	FAB+ 418 [M+H] ⁺ (20) 221 (40) 151 (30)	
2-98		127.5~ 128.5 °C	CDCl ₃ , 300 MHz 7.05 (1H, d, J=8.4 Hz) 7.02 (2H, d, J=8.5 Hz) 6.75 (2H, d, J=8.5 Hz) 6.74 (1H, d, J=8.4 Hz) 6.46 (1H, bs) 6.30 (1H, bs) 4.50 (1H, bs) 3.94 (2H, t, J=6.7 Hz) 3.89 (2H, q, J=5.6 Hz) 3.83 (3H, s) 3.64 (2H, q, J=6.9 Hz) 2.95 (2H, t, J=5.6 Hz)	3152 1943 1623 1543 1489 1279	FAB+ 402 [M+H] ⁺ (100)	C ₂₃ H ₃₁ NO ₅ Calcd. C: 68.81% H: 7.78% N: 3.49% Found C: 68.34% H: 7.70% N: 3.53%
2-99			CDCl ₃ , 300 MHz 7.17 (2H, d, J=5.7 Hz) 7.11 (2H, d, J=8.5 Hz) 6.92 (1H, bs) 6.78 (2H, d, J=8.5 Hz) 3.93 (2H, t, J=6.7 Hz) 3.89 (2H, q, J=5.7 Hz) 3.84 (3H, s) 3.71 (2H, q, J=6.7 Hz) 2.95 (2H, t, J=6.7 Hz) 2.92 (2H, t, J=5.7 Hz) 1.7-1.8 (2H, m) 1.70 (1H, bs)	Neat 3247 2935 1631 1596 1558 1488 1278 1086	FAB+ 387 [M+H] ⁺ (90) 106 (100)	C ₂₂ H ₃₀ N ₂ O ₄ Calcd. C: 68.37% H: 7.82% N: 7.25% Found C: 68.37% H: 7.75% N: 7.39%

Table 79

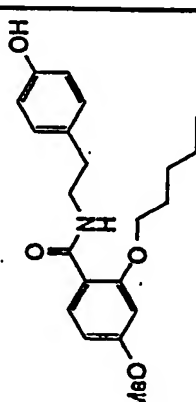
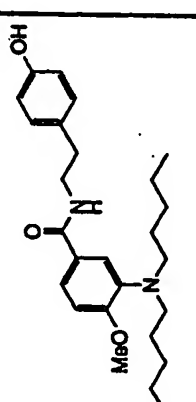
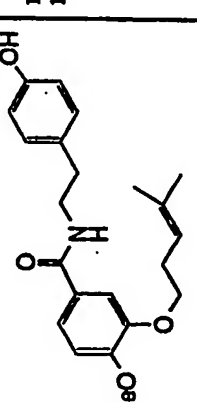
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-100	 <p>Colorless crystals</p>	96.6~ 97.2°C	CDCl ₃ , 300MHz 8.19(1H, d, J=8.7 Hz) 8.02(1H, br) 7.07(2H, d, J=8.4 Hz) 6.79(2H, d, J=8.4 Hz) 6.58(1H, dd, J=8.7, 2.1 Hz) 7.08(2H, d, J=8.0 Hz) 6.92(1H, d, J=8.0 Hz) 6.43(1H, d, J=2.1 Hz) 5.72(1H, s) 3.99(2H, t, J=6.6 Hz) 3.83(3H, s) 3.69(2H, q, J=6.7 Hz)		FAB+ 358 [M ⁺ H] ⁺ (100) 221(20)	
2-101			CDCl ₃ , 300MHz 7.39(1H, d, J=2.4 Hz) 7.22(1H, dd, J=8.4, 2.4 Hz) 7.05(2H, d, J=8.4 Hz) 6.81(2H, d, J=8.4 Hz) 6.79(1H, d, J=8.4 Hz) 6.17(1H, br) 3.85(3H, s) 3.65(2H, q, J=6.6 Hz) 3.06(4H, t, J=7.8 Hz) 2.83(2H, t, J=7.1 Hz) 1.13-1.50(12H, m) 0.84(6H, t, J=6.8 Hz)		FAB+ 427 [M ⁺ H] ⁺ (90) 369(100)	
2-102	 <p>Colorless crystals</p>	120.6~ 121.1°C	CDCl ₃ , 300MHz 7.35(1H, d, J=2.0 Hz) 7.16(1H, dd, J=8.1, 2.0 Hz) 7.07(2H, d, J=8.5 Hz) 6.83(2H, d, J=8.5 Hz) 6.80(1H, d, J=8.4 Hz) 6.08(1H, br) 5.83(1H, br) 5.1-5.2(1H, m) 4.00(2H, t, J=7.4 Hz) 3.89(3H, s) 3.66(2H, q, J=6.9 Hz) 2.84(2H, t, J=6.9 Hz)	Neat 3320 1510 1266	FAB+ 370 [M ⁺ H] ⁺ (100)	C ₂₂ H ₂₇ NO ₄ Calcd. C: 71.52% H: 7.37% N: 3.79% Found C: 71.82% H: 7.43% N: 3.90%

Table 80

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-103	<p>Colorless crystals</p>	131.9~ 132.1°C	CDCl_3 , 300MHz 7.35(1H, d, J=2.0 Hz) 7.13(1H, dd, J=8.4, 2.0 Hz) 7.06(2H, d, J=8.5 Hz) 6.81(1H, d, J=8.4 Hz) 6.79(1H, d, J=8.5 Hz) 6.00(1H, bs) 6.09(1H, bs) 3.99(2H, t, J=7.0 Hz) 3.87(3H, s) 3.64(2H, q, J=6.9 Hz) 2.83(2H, t, J=6.9 Hz) 1.7-1.9(2H, m)	KBr 3380 2954 1509 1267 1228	FAB+ 372[M ⁺ H] ⁺ (100) 235(60)	$\text{C}_{22}\text{H}_{29}\text{NO}_4$ Calcd. C: 71.13% H: 7.87% N: 3.77% Found C: 71.41% H: 7.93% N: 3.87%
2-104	<p>Colorless crystals</p>	115.3~ 116.0°C	CDCl_3 , 300MHz 7.36(1H, d, J=2.1 Hz) 7.21(1H, dd, J=8.4, 2.1 Hz) 7.10(2H, d, J=8.4 Hz) 6.82(2H, dd, J=8.4, 1.5 Hz) 6.05(1H, bs) 5.48(1H, s) 3.88(3H, s) 3.66(2H, q, J=6.6 Hz) 3.03(2H, t, J=7.7 Hz) 2.85(2H, t, J=7.1 Hz) 2.79(3H, s) 1.44-1.6(2H, m)		FAB+ 371 [M ⁺ H] ⁺ (100) 313(70)	
2-105	<p>Colorless crystals</p>	115.5~ 116.1°C	CDCl_3 , 300MHz 7.09(2H, d, J=8.4 Hz) 6.98(1H, d, J=1.8 Hz) 6.89(1H, dd, J=8.1, 1.8 Hz) 6.79(2H, d, J=8.4 Hz) 6.68(1H, d, J=8.1 Hz) 6.06(1H, bs) 5.46(1H, bs) 4.25(1H, bs) 4.0(2H, t, J=6.5 Hz) 3.65(2H, q, J=6.6 Hz) 3.14(2H, t, J=7.1 Hz) 2.84(2H, t, J=6.9 Hz)		FAB+ 412 [M ⁺ H] ⁺ (100) 276(40)	

Table 81

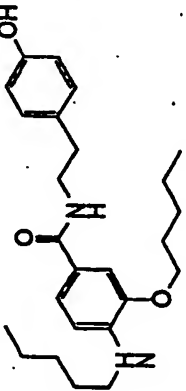
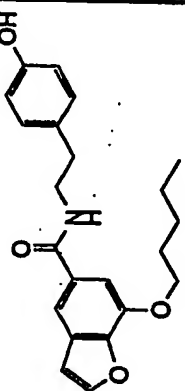
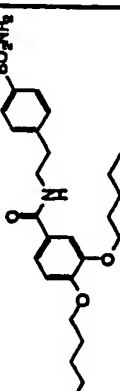
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-106	 <p>Pale-yellow crystals</p>	102.2 ~ 103.5 °C	CDCl ₃ , 300MHz 7.25 (1H, s) 7.07 (2H, d, J=8.4 Hz) 7.07 (1H, d, J=8.4 Hz) 6.78 (2H, d, J=8.4 Hz) 6.46 (1H, d, J=8.4 Hz) 5.98 (1H, br) 5.31 (1H, br) 4.53 (1H, br) 4.01 (2H, t, J=6.6 Hz) 3.63 (2H, q, J=6.6 Hz) 3.14 (2H, t, J=7.1 Hz) 2.82 (2H, t, J=6.8 Hz)		FAB+ 413 [M ⁺ H] ⁺ (70) 276 (100)	
2-107	 <p>Yellow oil</p>		CDCl ₃ , 300MHz 7.64 (1H, d, J=2.2 Hz) 7.42 (1H, d, J=1.5 Hz) 7.26 (1H, d, J=1.5 Hz) 7.05-7.08 (2H, m) 6.80-6.83 (2H, m) 6.73-6.74 (1H, d, J=2.2 Hz) 6.52 (1H, brs) 6.29 (1H, brt) 4.16 (2H, t, J=6.8 Hz) 3.68 (2H, q, J=6.8 Hz) 2.85 (2H, t, J=6.8 Hz)	2932 1595 1314 1341 1203	FAB+ 368 [M+H] ⁺ (100) 231 (90)	C ₂₂ H ₂₅ NO ₄ Calcd. C: 71.91% H: 6.86% N: 3.81% Found C: 71.00% H: 6.92% N: 3.54%
2-108	 <p>Colorless flakes</p>	187.0 ~ 187.5 °C	DMSO-d ₆ , 300MHz 8.40 (1H, br) 7.74 (2H, d, J=8.3 Hz) 7.42 (2H, d, J=8.3 Hz) 7.3-7.5 (2H, m) 7.26 (2H, s) 6.70 (1H, d, J=9.0 Hz) 3.99 (2H, t, J=6.2 Hz) 3.97 (2H, t, J=6.2 Hz) 3.45 (2H, q, J=6.6 Hz) 2.91 (2H, t, J=7.1 Hz) 1.6-1.8 (4H, m) 1.3-1.5 (8H, m)	KBr 3399 2939 1628 1505 1268 1161	FAB+ 477 [M ⁺ H] ⁺ (100)	C ₂₈ H ₃₄ N ₂ O ₅ S Calcd. C: 63.00% H: 7.61% N: 5.88% Found C: 63.28% H: 7.60% N: 5.80%

Table 82

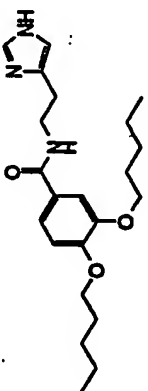
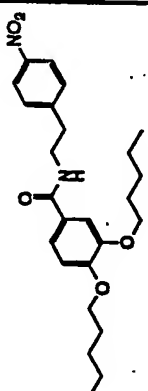
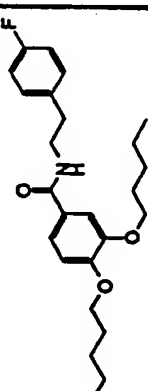
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-109		163.5 ~ 163.7°C	CDCl ₃ , 300MHz 7.58(1H, d, J=0.9 Hz) 7.43(1H, d, J=2.0 Hz) 7.29(1H, dd, J=8.3, 2.0 Hz) 7.30(1H, bc) 6.85(1H, d, J=8.3 Hz) 6.85(1H, d, J=0.9 Hz) 4.0-4.1(4H, m) 3.71(2H, q, J=6.3 Hz) 2.90(2H, t, J=6.3 Hz) 1.7-1.9(4H, m) 1.3-1.5(8H, m) 0.93(3H, t, J=7.0 Hz)	KBr 3201 2933 1632 1514 1268 1222	FAB+ 388 [M ⁺ H] ⁺ (100)	C ₂₂ H ₂₉ N ₃ O ₃ Calcd. C: 68.20% H: 8.58% N: 10.84% Found C: 68.23% H: 8.61% N: 10.66%
2-110		118.3 ~ 118.4°C	CDCl ₃ , 300MHz 8.17(2H, d, J=8.7 Hz) 7.40(2H, d, J=8.7 Hz) 7.35(1H, d, J=2.1 Hz) 7.13(1H, dd, J=8.4, 2.1 Hz) 6.83(1H, d, J=8.4 Hz) 6.10(1H, bc) 4.03(2H, t, J=6.6 Hz) 4.02(2H, t, J=6.6 Hz) 3.72(2H, q, J=7.0 Hz) 3.05(2H, t, J=7.0 Hz) 1.8-1.9(4H, m) 1.3-1.5(8H, m)	KBr 3497 3286 1750 1627 1522	FAB+ 443 [M ⁺ H] ⁺ (100)	C ₂₅ H ₂₉ N ₃ O ₃ Calcd. C: 67.85% H: 7.74% N: 6.33% Found C: 68.05% H: 7.87% N: 6.32%
2-111		105.8 ~ 106.4°C	CDCl ₃ , 300MHz 7.34(1H, d, J=2.1 Hz) 7.20(1H, d, J=8.7 Hz) 7.18(1H, d, J=8.7 Hz) 7.13(1H, dd, J=8.3, 2.1 Hz) 7.02(1H, d, J=8.7 Hz) 6.99(2H, d, J=8.6 Hz) 6.82(1H, d, J=8.3 Hz) 6.00(1H, bc) 4.02(2H, t, J=6.7 Hz) 4.01(2H, t, J=6.6 Hz) 3.66(2H, q, J=6.8 Hz) 2.89(2H, t, J=6.9 Hz)	KBr 3279 2931 1628 1510 1277	FAB+ 416 [M ⁺ H] ⁺ (100)	C ₂₂ H ₂₉ FNO ₃ • 1/2H ₂ O Calcd. C: 70.73% H: 8.31% N: 3.30% Found C: 70.70% H: 8.26% N: 3.26%

Table 83

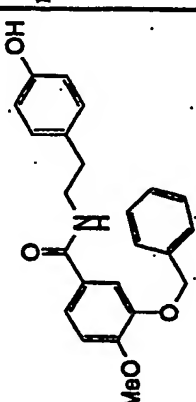
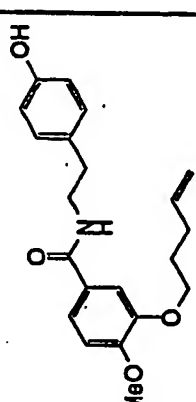
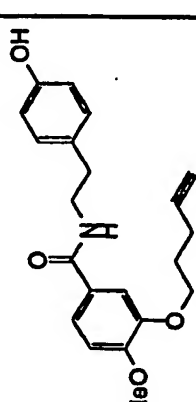
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR _{cm⁻¹}	MS	Elem. anal.
2-112	 <p>Colorless crystals</p>	132~133 °C	CDCl ₃ 300MHz 7.30-7.45 (6H, m) 7.18 (1H, dd, J=8.4, 2.2 Hz) 7.06-7.09 (2H, m) 6.84 (1H, d, J=8.4 Hz) 6.78-6.81 (2H, m) 5.99 (1H, brt) 5.32 (1H, s) 5.15 (2H, s) 3.90 (3H, s) 3.63 (2H, q, J=6.6 Hz) 2.83 (2H, t, J=6.6 Hz)		FAB+ 378 [M+H] ⁺ (27) 154(100)	
2-113						
2-114						

Table 84

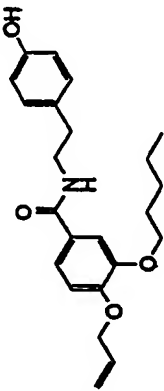
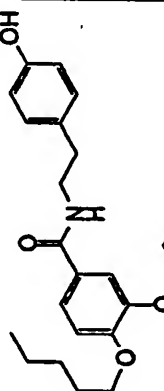
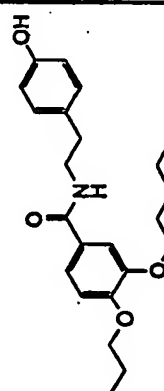
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-115	 <p>Colorless crystals</p>	114~116 °C	CDCl ₃ 300MHz 7.36 (1H, d, J=2.0 Hz) 7.06-7.12 (3H, m) 6.78-6.84 (3H, m) 6.00-6.10 (2H, m) 5.60 (1H, s) 5.26-5.44 (2H, m) 4.60-4.63 (3H, m) 4.02 (2H, t, J=6.8 Hz) 3.65 (2H, q, J=6.8 Hz) 2.84 (2H, t, J=6.8 Hz) 1.79-1.88 (2H, m) 1.30-1.50 (4H, m)		FAB+ 384[M+H+] (100) 263(29) 247(62)	
2-116	 <p>Colorless crystals</p>	139~139 °C	CDCl ₃ 300MHz 7.34 (1H, d, J=2.0 Hz) 7.16 (1H, dd, J=8.4, 2.0 Hz) 7.05-7.08 (2H, m) 6.79-6.84 (3H, m) 5.97-6.09 (3H, m) 5.24-5.43 (2H, m) 4.57-4.60 (2H, m) 4.02 (2H, t, J=6.7 Hz) 3.64 (2H, q, J=6.7 Hz) 2.83 (2H, t, J=6.7 Hz) 1.78-1.87 (2H, m)		FAB+ 384[M+H+] (100) 263(31) 247(48)	
2-117						

Table 85

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elen. anal.
2-118						
2-119		121.2~ 121.6°C	CDCl ₃ , 300MHz 7.3-7.5(5H, m) 7.16(2H, d, J=8.5 Hz) 7.09(1H, d, J=8.5 Hz) 6.94(2H, d, J=8.5 Hz) 6.77(1H, d, J=8.5 Hz) 6.20(1H, br) 5.05(2H, s) 4.66(2H, d, J=6.9 Hz) 4.17(1H, t, J=6.9 Hz) 3.98(4H, t, J=6.7 Hz) 3.70(2H, q, J=6.2 Hz) 2.88(2H, t, J=6.2 Hz)	KBr 3358 2953 1631 1511 1236	FAB+ 534 [M ⁺ H] ⁺ (20) 516(100)	C ₂₀ H ₂₄ NO ₃ Calcd. C: 74.27% H: 8.12% N: 2.62 % Found C: 74.54% H: 8.15% N: 2.67%
2-120		117.7- 118.7°C	CDCl ₃ , 300MHz 8.17(2H, d, J=8.7 Hz) 7.41(2H, d, J=8.7 Hz), 7.14(1H, d, J=8.5 Hz), 6.80(1H, d, J=8.5 Hz) 6.53(1H, br) 4.64(2H, s) 4.00(1H, br) 3.98(2H, t, J=6.3 Hz), 3.98(2H, t, J=6.7 Hz) 3.73(2H, q, J=6.9 Hz) 3.06(2H, t, J=6.9 Hz) 1.7-1.9(4H, m)	KBr 3281 2958 1628 1522 1348	FAB+ 473 [M+H] ⁺ (10), 455(100)	C ₂₆ H ₃₆ N ₂ O ₆ Calcd. C: 66.08% H: 7.68% N: 5.93% Found C: 66.38% H: 7.73% N: 5.88%

Table 86

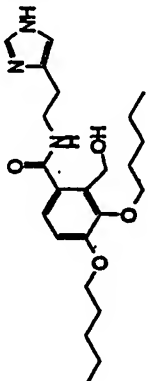
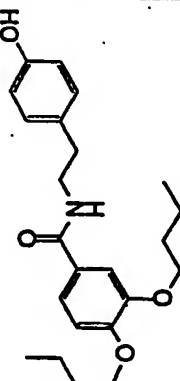
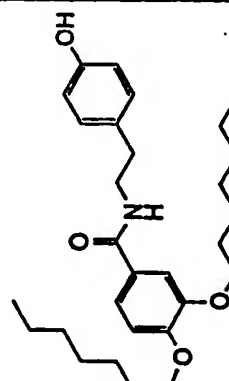
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-121	 <p>Colorless crystals</p>	128.4~ 128.8 °C	CDCl ₃ , 300MHz 7.60(1H, s) 7.48(1H, bs) 7.33(1H, d, J=8.5 Hz) 7.33(1H, s) 6.90(1H, s) 6.88(1H, d, J=8.5 Hz) 4.77(2H, s) 4.70(1H, bs) 4.05(2H, t, J=6.6 Hz) 4.05(2H, t, J=6.6 Hz) 3.75(2H, q, J=6.0 Hz) 2.96(2H, t, J=6.0 Hz)	KBr 3205 2932 1618 1569 1276	FAB+ 418 [M+H] ⁺ (30) 400(100)	C ₂₃ H ₂₉ N ₃ O ₄ Calcd. C: 66.16% H: 8.45% N: 10.06% Found C: 66.36% H: 8.52% N: 9.81%
2-122	 <p>Colorless crystals</p>	133~134 °C	CDCl ₃ , 300MHz 7.34 (1H, d, J=1.8 Hz) 7.12 (1H, dd, J=8.2, 1.8 Hz) 7.07-7.10 (2H, m) 6.77-6.84 (3H, m) 6.05 (1H, m) 5.40 (1H, s) 4.02 (4H, t, J=6.6 Hz) 3.65 (2H, q, J=6.7 Hz) 2.85 (2H, t, J=6.7 Hz) 1.75-1.85 (4H, m) 1.44-1.59 (4H, m)	0.95-1.00 (6H, m)	FAB+ 386[M+H] ⁺ (100)	
2-123	 <p>Colorless crystals</p>	124~125 °C	CDCl ₃ , 300MHz 7.34 (1H, d, J=2.2 Hz) 7.07-7.26 (3H, m) 6.78-6.83 (3H, m) 6.06 (1H, t, J=6.6 Hz) 5.53 (1H, s) 4.01 (4H, t, J=6.6 Hz) 3.65 (2H, q, J=6.6 Hz) 2.84 (2H, t, J=6.6 Hz) 1.74-1.88 (4H, m) 1.22-1.52 (16H, m) 0.89 (6H, t, J=7.0 Hz)		FAB+ 470[M+H] ⁺ (100)	

Table 87

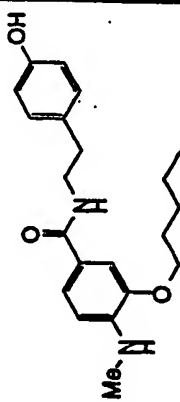
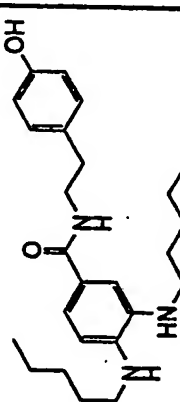
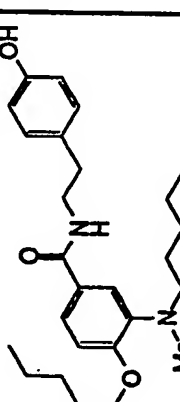
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-124	 <p>Colorless crystals</p>	215.1~ 215.7°C	DMSO-d ₆ , 300MHz 9.12(1H, s) 8.09(1H, bt) 7.35(1H, d, J=8.4 Hz) 7.24(1H, d, J=1.5 Hz) 7.0(2H, d, J=8.1 Hz) 6.65(2H, d, J=8.1 Hz) 6.43(1H, d, J=8.4 Hz) 5.34(1H, q, J=2.7 Hz) 3.96(2H, t, J=6.6 Hz) 3.34(2H, q, J=7.8 Hz) 2.74(3H, d, J=2.7 Hz) 2.67(2H, t, J=7.5 Hz)		FAB+ 357 [M ⁺ H] ⁺ (70) 220(100)	
2-125	 <p>Colorless crystals</p>	85.3~ 86.3°C	CDCl ₃ , 300MHz 7.14(1H, d, J=1.8 Hz) 7.08(2H, d, J=8.4 Hz) 7.06(1H, dd, J=7.8, 1.8 Hz) 6.78(2H, d, J=8.4 Hz) 6.56(1H, d, J=7.8 Hz) 6.03(1H, bt) 3.65(2H, q, J=6.6 Hz) 3.11(2H, t, J=6.8 Hz) 3.10(2H, t, J=6.8 Hz) 1.6-1.8(4H, m) 1.3-1.5(8H, m) 0.93(6H, t, J=7.1 Hz)		FAB+ 412 [M ⁺ H] ⁺ (40) 185(100)	
2-126	 <p>Colorless crystals</p>	109.4~ 110.4°C	CDCl ₃ , 300MHz 7.33(1H, d, J=2.4 Hz) 7.16(1H, dd, J=8.4 Hz) 7.09(2H, d, J=8.4 Hz) 6.75-6.82(3H, m) 6.04(1H, bt) 5.49(1H, bt) 4.00(2H, t, J=6.6 Hz) 3.65(2H, q, J=6.6 Hz) 3.04(2H, t, J=7.8 Hz) 2.84(2H, t, J=6.9 Hz) 2.80(3H, s) 1.8-1.95(2H, m)		FAB+ 427 [M ⁺ H] ⁺ (100) 369(50)	

Table 88

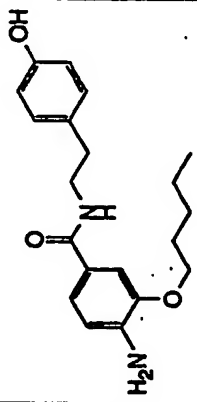
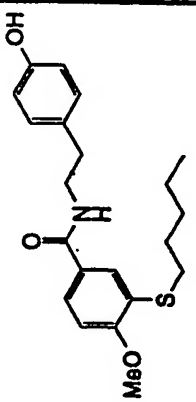
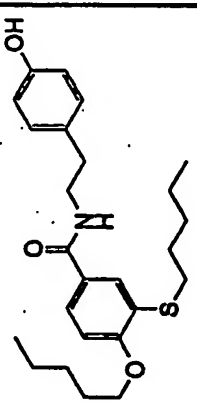
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm⁻¹}	MS	Elem. anal.
2-127	 <p>Colorless crystals</p>	138.5 ~ 139.5 °C	CDCl ₃ , 300MHz 7.29(1H, d, J=1.8 Hz) 7.08(2H, d, J=8.5 Hz) 7.00(1H, dd, J=8.1, 1.8 Hz) 6.79(2H, d, J=8.5 Hz) 6.61(1H, d, J=8.1 Hz) 6.00(1H, br) 5.40(1H, br) 4.09(2H, t, J=6.6 Hz) 4.02(2H, t, J=6.6 Hz) 3.64(2H, q, J=6.6 Hz) 2.83(2H, t, J=6.9 Hz) 1.75-1.9(2H, m)		FAB+ 343 [M ⁺ H] ⁺ (50) 185(100)	
2-128	 <p>Colorless crystals</p>	124.1 ~ 124.9 °C	CDCl ₃ , 300MHz 7.63(1H, d, J=2.1 Hz) 7.43(1H, dd, J=8.4, 2.1 Hz) 7.12(2H, d, J=8.4 Hz) 6.8(1H, d, J=8.4 Hz) 6.79(2H, d, J=8.4 Hz) 6.04(1H, br) 5.25(1H, s) 3.92(3H, s) 3.66(2H, q, J=6.5 Hz) 2.91(2H, t, J=7.4 Hz) 2.86(2H, t, J=6.9 Hz) 1.6-1.73(2H, m)		FAB+ 374 [M ⁺ H] ⁺ (100) 237(60)	
2-129	 <p>Colorless crystals</p>	116.3 ~ 116.9 °C	CDCl ₃ , 300MHz 7.62(1H, d, J=2.4 Hz) 7.41(1H, dd, J=8.7, 2.4 Hz) 7.09(2H, d, J=8.4 Hz) 6.8(2H, d, J=8.4 Hz) 6.78(1H, d, J=8.7 Hz) 6.02(1H, br) 5.16(1H, s) 4.04(2H, t, J=6.6 Hz) 3.66(2H, q, J=6.5 Hz) 2.90(2H, t, J=7.4 Hz) 2.85(2H, t, J=7.4 Hz) 1.8-1.9(2H, m)		FAB+ 430 [M ⁺ H] ⁺ (100) 305(50)	

Table 89

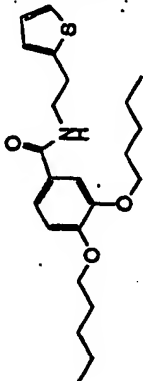
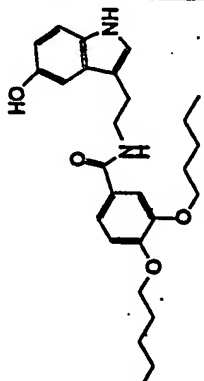
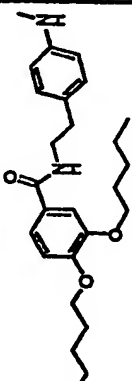
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm⁻¹}	MS	Elem. anal.
2-130			CDCl ₃ , 300MHz 7.35(1H, d, J=2.2 Hz) 7.16(1H, dd, J=8.3, 2.2 Hz) 7.17(1H, dd, J=5.1, 1.0 Hz) 6.95(1H, dd, J=5.1, 3.5 Hz) 6.85(1H, dd, J=3.5, 1.0 Hz) 6.15(1H, bs) 4.02(2H, t, J=6.7 Hz) 4.01(2H, t, J=6.6 Hz) 3.71(2H, q, J=6.5 Hz) 3.14(2H, t, J=6.5 Hz) 1.8-1.9(4H, m) 1.3-1.5(8H, m)			
2-131			CDCl ₃ , 300MHz 7.95(1H, s) 7.33(1H, d, J=2.1 Hz) 7.22(1H, d, J=8.7 Hz) 7.14(1H, dd, J=8.5, 2.1 Hz) 7.0-7.1(2H, m) 6.81(1H, dd, J=8.7, 2.5 Hz) 6.79(1H, d, J=6.8 Hz) 6.22(1H, bs) 5.50(1H, bs) 3.99(2H, t, J=6.6 Hz) 3.96(2H, t, J=6.3 Hz) 3.71(2H, q, J=6.5 Hz)		FAB+ 453 [M+H] ⁺ (30) 159(100) 277(80)	
2-132		130.7~ 131.0°C	CDCl ₃ , 300MHz 7.34(1H, d, J=2.1 Hz) 7.13(1H, dd, J=8.4, 2.1 Hz) 7.06(2H, d, J=8.5 Hz) 6.81(1H, d, J=8.4 Hz) 6.59(2H, d, J=8.5 Hz) 6.00(1H, bs) 4.02(2H, t, J=6.6 Hz) 4.00(1H, bs) 4.01(2H, t, J=6.6 Hz) 3.64(2H, q, J=6.7 Hz) 2.83(3H, s) 2.81(2H, t, J=6.7 Hz)	KBr 3370 2956 1624 1580 1523 1275 1225	FAB+ 427 [M+H] ⁺ (50), 277(100).	C ₂₆ H ₂₈ N ₂ O ₃ Calcd. C: 73.20% H: 8.96% N: 6.57% Found C: 73.28% H: 9.37% N: 6.55%

Table 90

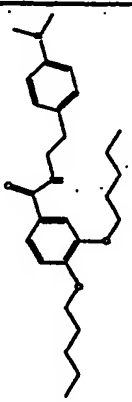
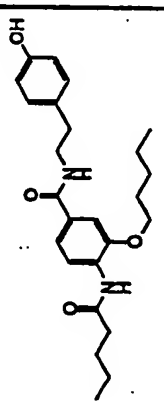
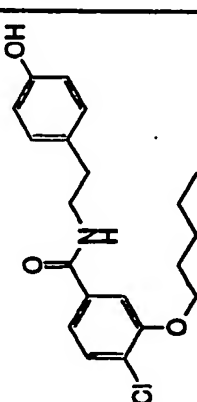
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-133		118.5~ 118.7°C	CDCl ₃ , 300MHz 7.34 (1H, d, J=2.1 Hz) 7.14 (1H, dd, J=8.4, 2.1 Hz) 7.11 (2H, d, J=8.7 Hz) 6.82 (1H, d, J=8.4 Hz) 6.71 (2H, d, J=8.7 Hz) 6.00 (1H, t) 4.02 (2H, t, J=6.6 Hz) 4.01 (2H, t, J=6.6 Hz) 3.65 (2H, q, J=6.7 Hz) 2.93 (6H, s) 2.82 (2H, t, J=6.7 Hz) 1.7-1.9 (4H, m)	KBr 3302 2956 1630 1511 1269 1226	FAB+ 441 [M+H+](50) 277(100)	
2-134		135.2~ 136.2°C	CDCl ₃ , 300MHz 8.40 (1H, d, J=8.4 Hz) 7.90 (1H, s) 7.44 (1H, d, J=1.8 Hz) 6.80 (2H, d, J=8.1 Hz) 7.1 (2H, d, J=8.1) 7.07 (1H, d, J=8.4 Hz) 6.12 (1H, t) 5.15 (1H, s) 4.10 (2H, t, J=6.6 Hz) 3.66 (2H, q, J=6.6 Hz) 2.85 (2H, t, J=7.1 Hz) 2.42 (2H, t, J=7.5 Hz)		FAB+ 427 [M+H+](100) 290(65)	
2-135		130.5~ 131.3°C	CDCl ₃ , 300MHz 7.38 (1H, d, J=1.7 Hz) 7.34 (1H, d, J=8.2 Hz) 7.09 (2H, d, J=8.3 Hz) 7.02 (1H, dd, J=2.1, 8.2 Hz) 6.78 (2H, d, J=8.3 Hz) 6.05 (1H, t) 4.96 (1H, s) 4.06 (2H, t, J=6.6 Hz) 3.67 (2H, q, J=6.0 Hz) 2.86 (2H, t, J=6.9 Hz) 1.8-1.92 (2H, m) 1.35-1.6 (4H, m)		FAB+ 362 [M+H+](60) 225(30)	

Table 91

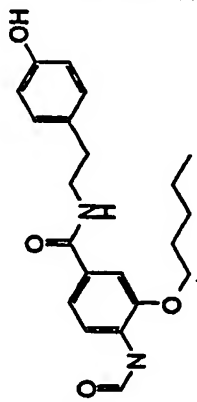
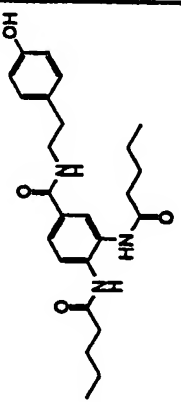
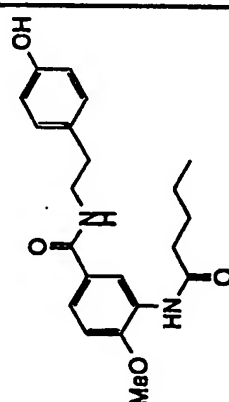
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-136	 <p>Colorless crystals</p>	177.9~ 178.2°C	CDCl ₃ , 300MHz 9.62(1H, br) 9.15(1H, s) 8.43(1H, br) 8.37(1H, br) 8.24(1H, d, J=8.4 Hz) 7.45(1H, br) 7.40(1H, d, J=8.4 Hz) 7.01(2H, d, J=8.1 Hz) 6.67(2H, d, J=8.1 Hz) 4.07(2H, t, J=6.6 Hz) 3.38(2H, q, J=8.1 Hz) 2.70(2H, t, J=7.1 Hz)		FAB+ 371 [M ⁺ H] ⁺ (30) 238(20)	
2-137	 <p>Colorless crystals</p>	179.0~ 179.8°C	DMSO-d ₆ , 300MHz 9.39(1H, br) 9.33(1H, br) 9.13(1H, br) 8.45(1H, br) 7.91(1H, br) 7.67(1H, d, J=8.4 Hz) 7.59(1H, d, J=8.4 Hz) 7.02(2H, d, J=8.7 Hz) 6.67(2H, d, J=8.7 Hz) 3.38(2H, br) 2.69(2H, t, J=7.4 Hz) 2.34(4H, t, J=7.4 Hz)		FAB+ 440 [M ⁺ H] ⁺ (50) 356(70)	
2-138	 <p>Colorless crystals</p>	126.9~ 127.6°C	CDCl ₃ , 300MHz 8.66(1H, s) 7.77(1H, br) 7.69(1H, dd, J=2.2, 8.5 Hz) 7.08(2H, d, J=8.4 Hz) 6.92(1H, d, J=8.5 Hz) 7.68(2H, d, J=8.4 Hz) 6.37(1H, br) 5.55(1H, s) 3.93(3H, s) 3.61(2H, q, J=6.7 Hz) 2.83(2H, t, J=7.1 Hz) 2.42(2H, t, J=7.5 Hz)		FAB+ 371 [M ⁺ H] ⁺ (60) 234(100)	

Table 92

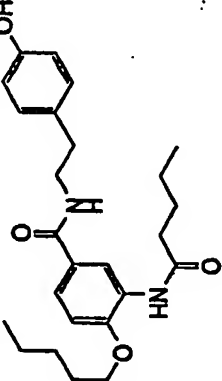
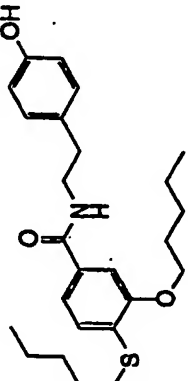
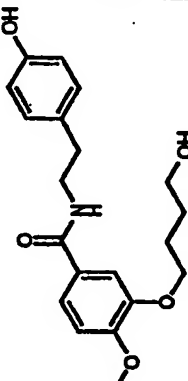
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-139	 Colorless crystals	164.1 ~ 164.8 °C	CDCl ₃ , 300MHz 8.64(1H, d, J=2.1 Hz) 7.80(1H, bs) 7.67(1H, dd, J=2.4, 9.0 Hz) 7.09(2H, d, J=8.4 Hz) 6.91(1H, d, J=9.0 Hz) 6.78(2H, d, J=8.4 Hz) 6.36(1H, bt) 5.59(1H, bs) 4.08(2H, t, J=6.6 Hz) 3.61(2H, q, J=6.7 Hz) 2.83(2H, t, J=6.9 Hz) 2.42(2H, t, J=7.5 Hz)		FAB+ 427 [M ⁺ H] ⁺ (40) 195(100)	
2-140	 Colorless crystals	130.3 ~ 131.4 °C	CDCl ₃ , 300MHz 7.26(1H, d, J=1.8 Hz) 7.05-7.15(4H, m) 6.80(2H, d, J=8.4 Hz) 6.05(1H, bs) 4.81(1H, s) 4.06(2H, t, J=6.6 Hz) 3.66(2H, q, J=6.6 Hz) 2.89(2H, t, J=7.4 Hz) 2.86(2H, t, J=6.8 Hz) 1.63-1.8(4H, m) 1.3-1.55(8H, m) 0.94(3H, t, J=6.9 Hz)	0.90(3H, t, J=7.2 Hz)	FAB+ 430 [M ⁺ H] ⁺ (100) 293(30)	
2-141	 Pale-red crystals	167.0 ~ 167.9 °C	DMSO-d ₆ , 300MHz 8.36(1H, t, J=5.4 Hz) 7.41(1H, dd, J=8.4, 2.1 Hz) 7.40(1H, d, J=2.1 Hz) 7.00(2H, d, J=8.4 Hz) 6.98(1H, d, J=8.4 Hz) 6.66(2H, d, J=8.4 Hz) 4.02(2H, t, J=6.6 Hz) 3.78(3H, s) 3.37(2H, q, J=6.6 Hz) 2.69(2H, t, J=6.6 Hz) 2.58(2H, t, J=6.6 Hz) 2.26(3H, s)	KBr 3325 1510	FAB+ 359[M+H] ⁺ (100).	C ₂₀ H ₂₅ NO ₅ Calcd. C: 66.83% H: 7.01% N: 3.89% Found C: 66.68% H: 7.10% N: 3.80%

Table 93

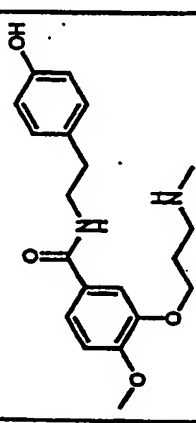
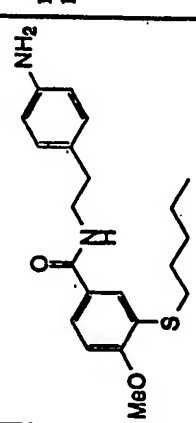
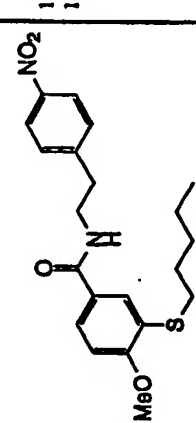
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
2-142	 <p>Colorless crystals</p>	169.0~ 170.0°C	DMSO-d ₆ , 300MHz 8.36 (1H, t, J=5.4 Hz) 7.41 (1H, dd, J=8.4, 2.1 Hz) 7.40 (1H, d, J=2.1 Hz) 7.00 (2H, d, J=8.4 Hz) 6.98 (1H, d, J=8.4 Hz) 6.66 (2H, d, J=8.4 Hz) 4.02 (2H, t, J=6.6 Hz) 3.78 (3H, s) 3.37 (2H, q, J=6.6 Hz) 2.69 (2H, t, J=6.6 Hz) 2.58 (2H, t, J=6.6 Hz) 2.26 (3H, s)	KBr 3500 1635 1516	FAB+ 359[M+H] ⁺ (100).	C ₂₂ H ₂₆ N ₂ O ₄ Calcd. C: 67.01% H: 7.31% N: 7.81% Found C: 62.45% H: 6.99% N: 7.23%
2-143	 <p>Colorless crystals</p>	139.1~ 140.1°C	CDCl ₃ , 300MHz 7.62 (1H, d, J=2.2 Hz) 7.42 (1H, dd, J=2.3, 8.5 Hz) 7.01 (2H, d, J=8.3 Hz) 6.79 (1H, d, J=8.5 Hz) 6.64 (2H, d, J=8.3 Hz) 5.98 (1H, br) 3.91 (1H, s) 3.63 (2H, q, J=6.4 Hz) 3.62 (2H, br) 2.90 (2H, t, J=7.4 Hz) 2.80 (2H, t, J=6.8 Hz) 1.55-1.7 (2H, m)		FAB+ 373 [M+H] ⁺ (30) 237 (50)	
2-144	 <p>Colorless crystals</p>	106.9~ 107.9°C	CDCl ₃ , 300MHz 8.19 (2H, d, J=9.0 Hz) 8.65 (1H, d, J=2.1 Hz) 7.44 (1H, dd, J=2.1, 8.4 Hz) 7.41 (2H, d, J=9.0 Hz) 6.82 (1H, d, J=8.4 Hz) 6.05 (1H, br) 3.93 (3H, s) 3.74 (2H, q, J=6.6 Hz) 3.07 (2H, t, J=6.9 Hz) 2.92 (2H, t, J=7.5 Hz) 1.6-1.75 (2H, m) 1.3-1.5 (4H, m)		FAB+ 403 [M+H] ⁺ (30) 307 (20)	

Table 94

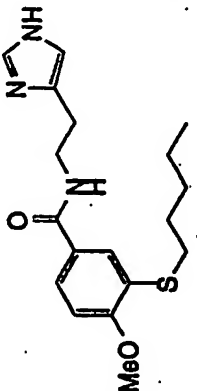
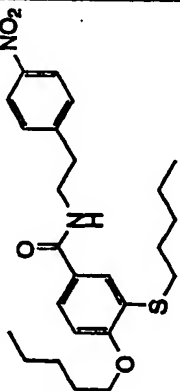
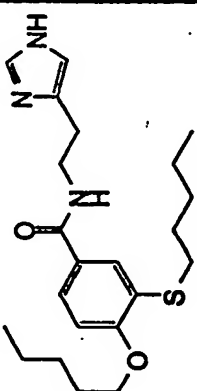
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
2-145	 <p>Colorless crystals</p>	132.2~ 132.6°C	CDCl ₃ , 300MHz 7.75(1H, d, J=2.1 Hz) 7.60(1H, s) 7.59(1H, d, J=8.4 Hz) 7.38(1H, bs) 6.87(1H, s) 6.84(1H, d, J=8.4 Hz) 3.93(3H, s) 3.73(2H, q, J=6.0 Hz) 2.86-3.0(4H, m) 1.63-1.75(2H, m) 1.3-1.5(4H, m) 0.89(3H, t, J=7.2 Hz)		FAB+ 348 [M ⁺ H ⁺] (80) 237(30)	
2-146	 <p>Colorless crystals</p>	106.4~ 107.2°C	CDCl ₃ , 300MHz 8.19(2H, d, J=9.0 Hz) 7.64(1H, d, J=2.4 Hz) 7.42(1H, dd, J=2.7, 8.7 Hz) 7.41(2H, d, J=9.0 Hz) 6.80(1H, d, J=8.7 Hz) 6.04(1H, bs) 4.06(2H, t, J=6.5 Hz) 3.73(2H, q, J=6.6 Hz) 3.06(2H, t, J=6.9 Hz) 2.91(2H, t, J=7.4 Hz) 1.82-1.92(2H, m) 1.63-1.73(2H, m)		FAB+ 459 [M ⁺ H ⁺] (90) 293(40)	
2-147	 <p>Colorless crystals</p>	133.2~ 134.1°C	CDCl ₃ , 300MHz 7.72(1H, d, J=2.2 Hz) 7.59(1H, s) 7.55(1H, dd, J=2.2, 8.5 Hz) 7.31(1H, bs) 6.85(1H, s) 6.80(1H, d, J=8.5 Hz) 4.04(2H, t, J=6.6 Hz) 3.71(2H, q, J=5.9 Hz) 2.92(2H, t, J=7.3 Hz) 2.90(2H, t, J=6.5 Hz) 1.78-1.88(2H, m) 1.62-1.73(2H, m)		FAB+ 404 [M ⁺ H ⁺] (100) 293(40)	

Table 95

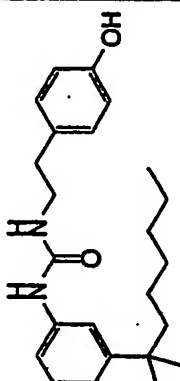
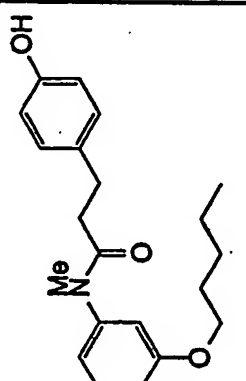
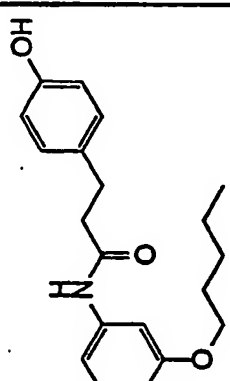
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
2-148						
2-149	 Amorphous		CDCl ₃ , 300MHz 0.95 (3H, t, J=7.00 Hz) 1.30 - 1.50 (4H, m) 1.79 (2H, q, J=7.12 Hz) 2.38 (2H, t, J=7.61 Hz) 2.84 (2H, t, J=7.67 Hz) 3.24 (3H, s) 3.92 (2H, t, J=6.59 Hz) 5.66 (1H, s) 6.58 - 6.63 (2H, m) 6.72 (2H, d, J=8.34 Hz) 6.85 (1H, dd, J=2.21, 8.41 Hz)	3287 3014 2933 2871 1633 1588 1516	FAB+ 342[M+H+] (100) 282(13)	
2-150	 Colorless crystals	83.9~ 84.2°C	CDCl ₃ , 300MHz 0.92 (3H, t, J=7.5 Hz) 1.32 - 1.45 (4H, m) 1.76 (2H, q, J=7.5 Hz) 2.60 (2H, t, J=7.5 Hz) 2.96 (2H, t, J=7.5 Hz) 3.92 (2H, t, J=6.0 Hz) 5.42 (1H, br) 6.65 (1H, d, J=6.0 Hz) 6.75 (2H, d, J=6.0 Hz) 6.85 (1H, d, J=6.0 Hz) 7.07 (2H, d, J=6.0 Hz) 7.13-7.26 (1H, m)	3092 2935 2867 1654 1620 1597	FAB+ 328[M+H+] (100) 282(13) 258(12)	C ₂₀ H ₂₅ NO ₃ Calcd. C: 73.37% H: 7.70% N: 4.28% Found C: 73.22% H: 7.94% N: 4.30%

Table 96

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR _{cm⁻¹}	MS	Elem. anal.
2-151	<p>Colorless crystals</p>	100.2~ 100.6°C	CDCl ₃ 300MHz 0.92 (3H, t, J=7.08 Hz) 6.90 (2H, d, J=8.43 Hz) 1.30 - 1.50 (4H, m) 1.75-1.88 (2H, m) 2.35 (2H, t, J=7.61 Hz) 2.81 (2H, t, J=7.67 Hz) 3.21 (2H, s) 3.86 (3H, s) 3.92 (2H, t, J= 6.83 Hz) 6.33 (1H, br) 6.52-6.56 (2H, m) 6.72 (2H, d, J=8.46 Hz) 6.80 (1H, d, J= 8.34 Hz)	3272 2933 2870 1630 1593 1514		
2-152	<p>Colorless crystals</p>		CDCl ₃ 300MHz 0.93 (3H, t, J=7.02 Hz) 7.69 (1H, d, J=15.45Hz) 1.27-1.48 (4H, m) 1.78 (2H, q, J=7.17 Hz) 3.97 (2H, t, J=6.59 Hz) 5.43 (1H, s) 6.39 (1H, d, J=15.43Hz) 6.68 (1H, dd, J=1.90, 7.81 Hz) 6.85 (2H, d, J= 8.61 Hz) 6.96-7.04 (1H, m) 7.18-7.26 (2H, m) 7.41-7.45 (3H, m)	3302 2954 1661 1603 1544	FAB+ 326[M+H+] (100) 284(47) 180(29)	C ₂₀ H ₂₃ NO ₃ Calcd. C: 73.82% H: 7.12% N: 4.30% Found C: 73.16% H: 7.28% N: 4.53%
2-153	<p>Colorless crystals</p>	121.6~ 121.9°C	CDCl ₃ 500MHz 0.91 (3H, t, J=7.3 Hz) 1.34-1.47 (4H, m) 1.79 (2H, q, J=7.0 Hz) 3.39 (3H, s) 3.96 (2H, t, J=6.5 Hz) 6.26 (1H, d, J=15.5 Hz) 6.36 (1H, br) 6.76-6.80 (4H, m) 6.89 (1H, d, J=8.5 Hz) 7.21 (2H, d, J=8.0 Hz) 7.31 (1H, t, J=6.3 Hz) 7.61 (1H, d, J=15.5 Hz)	3168 2935 2871 1644 1581	FAB+ 340[M+H+] (100) 233(34) 193(17)	C ₂₁ H ₂₅ NO ₃ Calcd. C: 74.31% H: 7.17% N: 4.13% Found C: 74.54% H: 7.54% N: 6.82%

Table 97

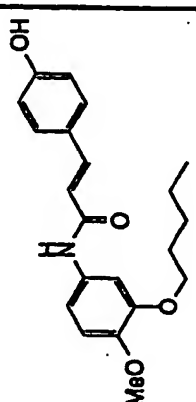
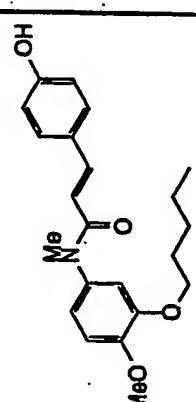
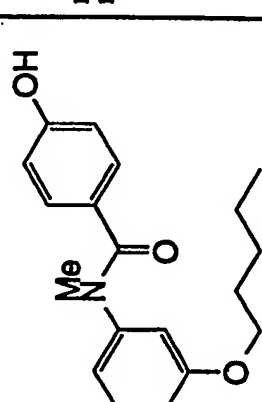
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
2-154	 <p>Colorless crystals</p>	177.7~ 178.0°C	DMSO-d ₆ 300MHz 0.89 (3H, t, J=7.5 Hz) 1.25-1.44 (4H, m) 1.72 (2H, q, J=6.0 Hz) 3.71 (3H, s) 3.90 (2H, t, J=7.5 Hz) 6.55 (1H, d, J=18.0 Hz) 6.81 (2H, d, J=6.0 Hz) 6.89 (1H, d, J=6.0 Hz) 7.16 (1H, d, J=6.0 Hz) 7.28-7.50 (4H, m) 9.88 (1H, s) 9.90 (1H, s)	3392 2956 1654 1605 1584 1510	FAB+ 356 [M+H] ⁺ (58) 314(100) 209(69)	C ₂₁ H ₂₅ NO ₄ Calcd. C: 70.96% H: 7.09% N: 3.94% Found C: 70.54% H: 7.04% N: 4.18%
2-155	 <p>Colorless crystals</p>	169.1~ 169.4°C	CDCl ₃ 300MHz 0.89 (3H, t, J=7.5 Hz) 1.28-1.46 (4H, m) 1.81 (2H, q, J=5.3 Hz) 3.37 (3H, s) 3.91 (3H, s) 3.97 (2H, t, J=7.5 Hz) 6.23 (1H, d, J=15.0 Hz) 6.73-6.90 (5H, m) 7.19 (2H, d, J=9.0 Hz) 7.60 (1H, d, J=15.0 Hz) 7.74 (1H, s)	3074 2933 1642 1578 1509	FAB+ 370 [M+H] ⁺ (74) 223(46) 147(100)	C ₂₂ H ₂₇ NO ₄ Calcd. C: 71.52% H: 7.37% N: 3.79% Found C: 71.32% H: 7.38% N: 3.70%
2-156	 <p>Colorless crystals</p>	152.7~ 152.9°C	CDCl ₃ 300MHz 0.92 (3H, t, J=7.07 Hz) 1.31-1.42 (4H, m) 1.71 (2H, q, J=6.89 Hz) 3.46 (3H, s) 3.82 (2H, t, J=6.60 Hz) 6.53-6.75 (5H, m) 7.11-7.17 (3H, m) 7.45 (1H, s)	3127 2937 1575 1518	FAB+ 314[M+H] ⁺ (100) 220(10) 193(27)	Calcd. C: 72.82% H: 7.40% N: 4.34% Found C: 72.15% H: 7.40% N: 4.44%

Table 98

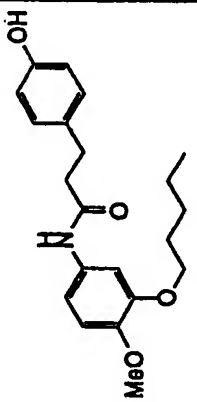
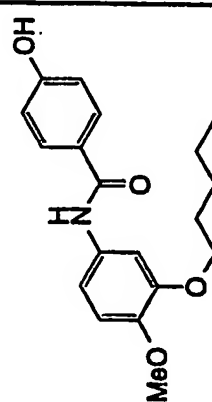
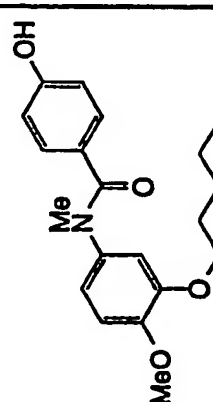
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
2-157	 <p>Colorless crystals</p>	125.8~ 126.1°C	CDCl ₃ 300MHz 0.91 (3H, t, J=7.5 Hz) 1.27-1.44 (4H, m) 1.82 (2H, q, J=7.5 Hz) 2.59 (2H, d, J=7.5 Hz) 2.97 (2H, d, J=7.5 Hz) 3.82 (3H, s) 3.98 (2H, t, J=7.5 Hz) 5.28 (1H, s) 6.73-6.78 (4H, m) 6.97 (1H, br) 7.08 (2H, d, J=7.5 Hz) 7.23 (1H, br)	3406 3240 3145 3085 2930 2865 1649 1613 1553 1512	FAB+ 358 [M+H] ⁺ (83) 357(100) 288(13) 209(23)	C ₂₁ H ₂₇ NO ₄ Calcd. C: 70.56% H: 7.61% N: 3.92% Found C: 70.57% H: 7.88% N: 3.96%
2-158	 <p>Colorless crystals</p>	137.7~ 138.0°C	CDCl ₃ 500MHz 0.90 (3H, t, J=7.0 Hz) 1.30-1.43 (4H, m) 1.73 (2H, q, J=6.9 Hz) 3.73 (3H, s) 3.91 (2H, t, J=6.5 Hz) 6.84 (2H, d, J=7.5 Hz) 6.89 (1H, d, J=9.0 Hz) 7.29 (1H, d, J=9.0 Hz) 7.44 (1H, br) 7.83 (2H, d, J=7.5 Hz) 9.80 (1H, br) 10.05 (1H, br)	3314 3123 2957 2868 1643 1608 1585 1550 1514	FAB+ 384 [M+H] ⁺ (80) 329(100) 260(17) 209(36)	C ₁₉ H ₂₃ NO ₄ Calcd. C: 69.28% H: 7.04% N: 4.25% Found C: 69.03% H: 7.14% N: 5.56%
2-159	 <p>Colorless crystals</p>	138.7~ 138.9°C	CDCl ₃ 500MHz 0.91 (3H, t, J=7.0 Hz) 1.34-1.40 (4H, m) 1.67-1.74 (2H, m) 3.44 (3H, s) 3.78-3.95 (5H, m) 6.52-6.72 (5H, m) 7.13-7.16 (3H, m)	3154 2933 1615 1589 1571 1507	FAB+ 344[M+H] ⁺ (100) 343(99) 223(35)	C ₂₀ H ₂₅ NO ₄ Calcd. C: 69.95% H: 7.34% N: 4.08% Found C: 69.09% H: 7.42% N: 5.73%

Table 99

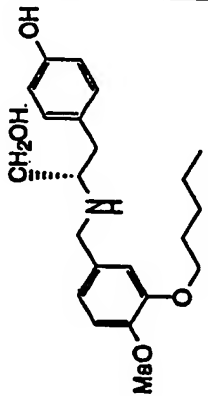
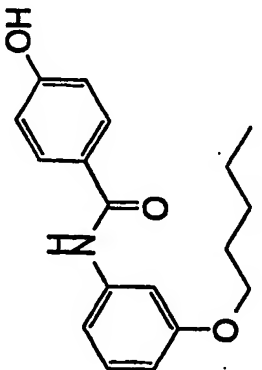
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRem ⁻¹	MS	Elem. anal.
2-160		257.1 ~ 258.2 °C	CDCl ₃ 300MHz 6.7-6.9 (7H, m) 4.70 (1H, bs) 3.94 (2H, t, J=6.8 Hz) 3.9-4.0 (2H, m) 3.80 (3H, s) 3.6-3.7 (2H, m) 3.4-3.5 (1H, m) 3.0-3.1 (2H, bs) 2.6-2.9 (2H, m) 1.7-1.8 (2H, m) 1.2-1.5 (4H, m) 0.88 (3H, t, J=7.0 Hz)	Neat 3288 2936 1515 1264	FAB+ 374 [M+H] ⁺ (30) 330(100)	
2-161	 Colorless crystals	101.6 ~ 101.8 °C	CDCl ₃ 300MHz 0.98 (3H, t, J=6.98 Hz) 1.38-1.52 (4H, m) 1.83 (2H, q, J=6.68 Hz) 4.01 (2H, t, J=6.51 Hz) 6.75 (1H, dd, J=2.21, 8.09 Hz) 6.93 (2H, d, J=8.61 Hz) 7.12 (1H, d, J=7.70 Hz) 7.28 (1H, t, J=8.04 Hz) 7.41-7.73 (2H, m) 7.76 (1H, d, J=8.54 Hz) 7.97 (1H, br)	3299 2938 2868 1640 1542 1508		C ₁₈ H ₂₁ NO ₃ Calcd. C; 72.22% H; 7.07% N; 4.68% Found C; 72.17% H; 7.15% N; 4.67%

Table 100

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
3-1		102.1~ 102.3 °C	CDCl ₃ , 300MHz 7.61(1H, d, J=15.9 Hz) 7.11(2H, d, J=8.5 Hz) 7.08(1H, dd, J=8.2, 1.9 Hz) 7.04(1H, d, J=1.9 Hz) 6.85(1H, d, J=8.2 Hz) 6.79(2H, d, J=8.5 Hz) 6.28 (1H, d, J=15.9 Hz) 5.20(1H, bs) 4.37(2H, t, J=7.1 Hz) 4.02(2H, t, J=6.9 Hz) 3.89(3H, s) 2.94(2H, t, J=7.1 Hz)	KBr 3449 1514 1260	FAB+ 385 [M+H] ⁺ (80) 384(100)	C ₁₇ H ₁₆ O ₂ Calcd. C: 71.85% H: 7.34% Found C: 72.22% H: 7.49%
3-2		104.1~ 104.3 °C	CDCl ₃ , 300MHz 7.63(1H, dd, J=8.4, 2.0 Hz) 7.51(1H, d, J=2.0 Hz) 7.14(2H, d, J=8.5 Hz) 6.87(1H, d, J=8.4 Hz) 6.78(2H, d, J=8.5 Hz) 6.50(1H, bs) 4.45(2H, t, J=7.0 Hz) 4.04(2H, t, J=6.9 Hz) 3.91(3H, s) 2.99(2H, t, J=6.9 Hz) 1.8-1.9(2H, m) 1.3-1.5(4H, m)	KBr 3377 2941 1687 1273	FAB+ 359 [M+H] ⁺ (30) 238(90) 221(95)	C ₁₇ H ₁₆ O ₂ Calcd. C: 70.37% H: 7.31% Found C: 70.55% H: 7.44%
3-3		170.1~ 171.2 °C	CDCl ₃ , 300MHz 8.1 (1H, d, J=9 Hz) 8.0 (1H, d, J=15 Hz) 7.4-8.0 3H, m) 7.2 (1H, d, J=9 Hz) 7.2 (1H, s) 6.9 (1H, d, J=9 Hz) 6.6 (1H, d, J=15 Hz) 4.1 (2H, t, J=4 Hz) 4.0 (3H, s) 1.8-2.0 (2H, m) 1.4-1.6 (4H, m) 1.0 (3H, t, J=7.5 Hz)	KBr 3448 2929 1777 1621 1595 1508 1260 1083	FAB+ 382 [M+H] ⁺ (20) 247(100)	C ₂₉ H ₂₃ N ₃ O ₄ Calcd. C: 66.13% H: 6.08% N: 11.02% Found C: 66.21% H: 6.09% N: 11.00%

Table 101

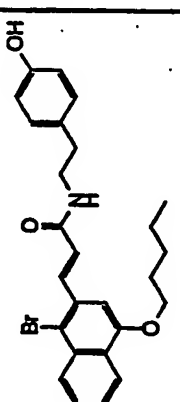
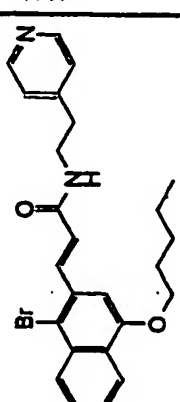
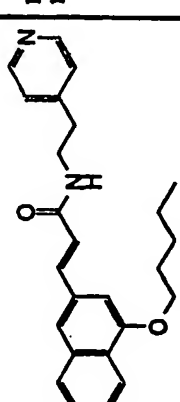
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^m	MS	Elem. anal.
4-1		205.4 ~ 206.0 °C	DMSO-d ₆ , 300MHz 9.15(1H, s) 8.17-8.30(3H, m) 7.98(1H, d, J=15.6 Hz) 7.72(1H, t, J=6.98 Hz) 7.64(1H, t, J=6.98 Hz) 7.15(1H, s) 7.14(2H, d, J=8.94 Hz) 6.80(1H, d, J=15.6 Hz) 6.69(2H, d, J=8.94 Hz) 4.23(2H, t, J=6.39 Hz) 3.39(2H, q, J=6.56 Hz) 2.69(2H, t, J=7.35 Hz)		FAB+ 483 [M ⁺ H] ⁺ (55) 485(30) 482(100)	
4-2		148.2 ~ 148.8 °C	DMSO-d ₆ , 300MHz 8.49(2H, d, J=5.97 Hz) 8.20-8.34(3H, m) 8.00(1H, d, J=15.6 Hz) 7.74(1H, t, J=7.70 Hz) 7.65(1H, t, J=7.70 Hz) 7.29(2H, d, J=5.97 Hz) 7.15(1H, s) 6.79(1H, d, J=15.6 Hz) 4.23(2H, t, J=6.42 Hz) 3.50(2H, q, J=6.34 Hz) 2.85(2H, t, J=7.0 Hz) 1.85-1.98(2H, m)		FAB+ 468 [M ⁺ H] ⁺ (20) 469(40) 467(45)	
4-3		148.3 ~ 149.5 °C	CDCl ₃ , 300MHz 8.76-8.82(1H, m) 8.55(2H, dd, J=4.2, 1.2 Hz) 8.22-8.37(1H, m) 7.74(1H, d, J=15.3 Hz) 7.45-7.54(3H, m) 7.26(1H, s) 7.18(2H, d, J=6.0 Hz) 6.89(1H, s) 6.39(1H, d, J=15.3 Hz) 5.67-5.75(1H, m) 4.15(2H, t, J=6.5 Hz) 3.71(2H, q, J=6.6 Hz)		FAB+ 389 [M ⁺ H] ⁺ (60) 307(30) 197(30)	

Table 102

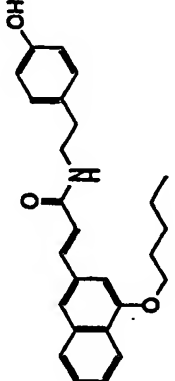
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
4-4		175.5~ 176.1°C	DMSO-d ₆ 300MHz 9.15(1H, s) 8.06-8.14(2H, m) 7.84-7.90(1H, m) 7.61(1H, s) 7.47-7.56(4H, m) 7.09(1H, s) 7.02(2H, d, J=8.4 Hz) 6.74(1H, d, J=15.6 Hz) 6.67(2H, d, J=8.4 Hz) 4.2(2H, t, J=6.45 Hz) 3.38(2H, q, J=6.8 Hz) 2.66(2H, t, J=7.35 Hz)		FAB+ 404 [M ⁺ H] ⁺ (60) 197(45)	

Table 103

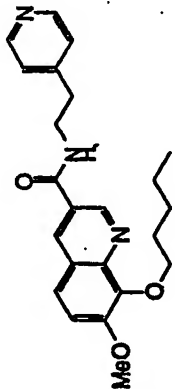
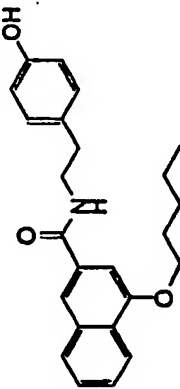
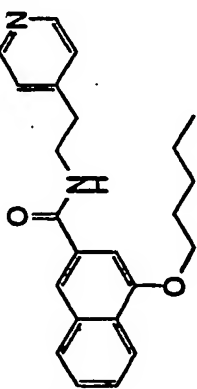
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
5-1			CDCl ₃ , 300MHz 9.15(1H, s) 8.51(1H, s) 8.50(2H, d, J=4.66 Hz) 7.61(1H, d, J=9.02 Hz) 7.40(1H, d, J=9.02 Hz) 7.17(2H, d, J=4.66 Hz) 6.64-6.75(1H, m) 4.26(2H, t, J=7.01 Hz) 4.03(3H, s) 3.80(2H, q, J=6.51 Hz) 2.99(2H, t, J=6.85 Hz) 1.80-1.95(2H, m)		FAB+ 394 [M ⁺ H ⁺](100) 336(25)	
5-2			CDCl ₃ , 300MHz 8.25-8.30(1H, m) 7.76-7.83(1H, m) 7.61(1H, s) 7.47-7.58(2H, m) 7.19(1H, s) 7.13(2H, d, J=8.3 Hz) 6.81(2H, d, J=8.3 Hz) 6.20-6.35(1H, m) 5.23(1H, s) 4.18(2H, t, J=6.44 Hz) 3.72(2H, q, J=6.56 Hz) 2.90(2H, t, J=6.92 Hz)		FAB+ 378 [M ⁺ H ⁺](80) 257(35) 241(50)	
5-3		103.6~ 105.4 °C	CDCl ₃ , 300MHz 8.55(1H, d, J=6.0 Hz) 8.25-8.31(1H, m) 7.77-7.83(1H, m) 7.63(1H, s) 7.50-7.57(2H, m) 7.21(1H, s) 7.20(2H, d, J=6.0 Hz) 6.30-6.45(1H, m) 4.19(2H, t, J=6.44 Hz) 3.78(2H, q, J=6.66 Hz) 3.00(2H, t, J=6.98 Hz) 1.89-2.00(2H, m)		FAB+ 363 [M ⁺ H ⁺](100) 305(15) 241(20)	

Table 104

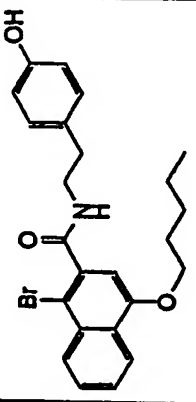
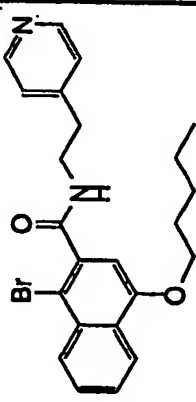
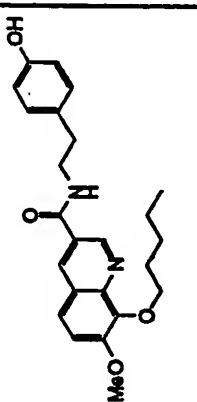
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
5-4		135.2~ 135.8°C	CDCl ₃ , 300MHz 8.28(1H, t, J=8.13 Hz) 8.25(1H, t, J=8.13 Hz) 7.64(1H, t, J=8.13 Hz) 7.55(1H, t, J=8.13 Hz) 7.15(2H, d, J=8.51 Hz) 6.80(1H, s) 6.78(2H, d, J=8.51 Hz) 5.92-6.03(1H, m) 4.89(1H, s) 4.11(2H, t, J=6.43 Hz) 3.76(2H, q, J=6.61 Hz) 2.93(2H, t, J=6.95 Hz)		FAB+ 457 [M ⁺ H] ⁺ (50) 458(90) 456(100)	
5-5		131.9~ 132.6°C	CDCl ₃ , 300MHz 8.54(2H, d, J=5.96 Hz) 8.28(1H, d, J=6.98 Hz) 8.25(1H, d, J=6.98 Hz) 7.65(1H, d, J=6.98 Hz) 7.55(1H, d, J=6.98 Hz) 7.23(2H, d, J=5.96 Hz) 6.80(1H, s) 6.02-6.16(1H, m) 4.11(2H, t, J=6.42 Hz) 3.82(2H, q, J=6.71 Hz) 3.03(2H, t, J=7.03 Hz) 1.87-2.00(2H, m)	136-1.62(4H, m) 0.94(3H, t, J=7.16 Hz)	FAB+ 442 [M ⁺ H] ⁺ (40) 443(80) 441(100)	
5-6	 Colorless crystals	141.2~ 142.6°C	DMSO-d ₆ , 300MHz 9.13(1H, d, J=2.4 Hz) 8.62(1H, d, J=2.4 Hz) 7.78(1H, d, J=9.9 Hz) 7.60(1H, d, J=9.9 Hz) 7.1(2H, d, J=8.7 Hz) 6.73(2H, d, J=8.7 Hz) 4.18(2H, t, J=6.8 Hz) 4.04(3H, s) 3.60(2H, t, J=7.4 Hz) 2.86(2H, t, J=7.4 Hz) 1.77-1.92(2H, m) 1.3-1.5(4H, m)	0.94(3H, t, J=7.2 Hz)	FAB+ 409 [M ⁺ H] ⁺ (100) 339(50)	

Table 105

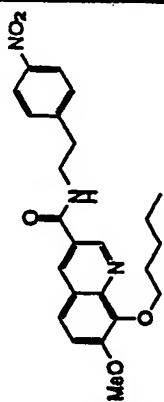
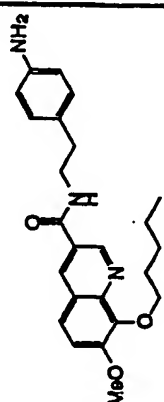
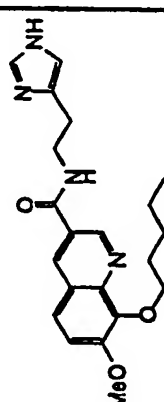
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
5-7	 <p>Pale-yellow crystals</p>	109.8~ 110.6°C	CDCl ₃ , 300MHz 9.12(1H, d, J=2.1 Hz) 8.50(1H, d, J=2.1 Hz) 8.20(2H, d, J=9.0 Hz) 7.64(1H, d, J=9.0 Hz) 7.43(2H, d, J=9.0 Hz) 7.42(1H, d, J=9.0 Hz) 6.29(1H, br) 4.27(2H, t, J=6.9 Hz) 4.04(3H, s) 3.83(2H, q, J=6.7 Hz) 3.12(2H, t, J=7.1 Hz) 1.83-1.95(2H, m)		FAB+ 438 [M ⁺ H] ⁺ (30) 307(20)	
5-8	 <p>Colorless crystals</p>	106.2~ 107.7°C	CDCl ₃ , 300MHz 9.11(1H, d, J=2.2 Hz) 8.51(1H, d, J=2.2 Hz) 7.65(1H, d, J=9.1 Hz) 7.42(1H, d, J=9.1 Hz) 7.07(2H, d, J=9.1 Hz) 6.70(2H, d, J=9.1 Hz) 6.22(1H, br) 4.29(2H, t, J=7.1 Hz) 4.05(3H, s) 3.75(2H, q, J=6.2 Hz) 3.65(2H, br) 2.88(2H, t, J=6.6 Hz)		FAB+ 408 [M ⁺ H] ⁺ (70) 307(20)	
5-9	 <p>Colorless crystals</p>	73.2~ 74.7°C	CDCl ₃ , 300MHz 9.34(1H, d, J=2.2 Hz) 8.67(1H, d, J=2.1 Hz) 8.30(1H, br) 7.75(1H, s) 7.68(1H, d, J=9.1 Hz) 7.41(1H, d, J=9.1 Hz) 6.92(1H, s) 4.29(2H, t, J=7.1 Hz) 4.05(3H, s) 3.75-3.86(2H, m) 2.85-2.95(2H, m) 1.8-1.95(2H, m)		FAB+ 383 [M ⁺ H] ⁺ (70) 307(20)	

Table 106

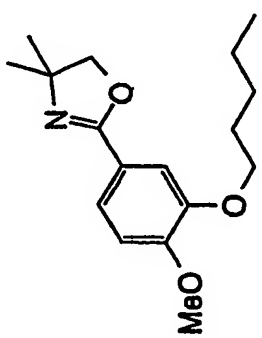
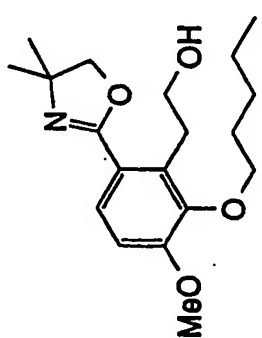
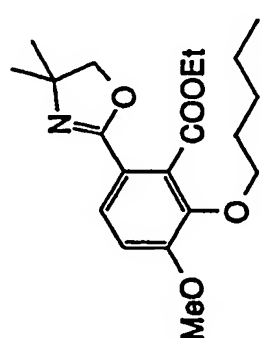
Ex.	Structural formula	n.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
6-1		62.0~ 63.2°C	CDCl ₃ , 300MHz 7.51(1H, dd, J=8.4, 1.8 Hz) 7.46(1H, d, J=1.8 Hz) 6.86(1H, d, J=8.4 Hz) 4.07(2H, s) 4.05 (2H, t, J=6.9 Hz) 3.89(3H, s) 1.8-2.0(2H, m) 1.3-1.5(4H, m) 1.37(6H, s) 0.93(3H, t, J=7.0 Hz)	Neat 2959 1648 1513	FAB+ 292 [M ⁺ H] ⁺ (100) 291(80) 276(75)	C ₁₇ H ₂₃ NO ₄ Calcd. C: 70.07 % H: 8.65 % N: 4.81 % Found C: 69.86 % H: 8.70 % N: 5.01 %
6-2			CDCl ₃ , 300MHz 7.5(1H, d, J=9.0 Hz) 6.89(1H, d, J=9.0 Hz) 6.2(1H, bs) 4.1(2H, s) 4.0(2H, t, J=7.5 Hz) 4.0(2H, t, J=4.5 Hz) 3.9(3H, s) 3.3(2H, t, J=4.5 Hz) 1.6-1.8(2H, m) 1.3-1.5(4H, m) 1.4(6H, s) 0.93(3H, t, J=7.5 Hz)	Neat 3264 2960 1640	FAB+ 336 [M ⁺ H] ⁺ (100) HRFAB(m/z) 336.2189 Calcd. C ₁₉ H ₂₅ NO ₄ 336.4558 Found 336.2189	C ₁₉ H ₂₅ NO ₄ Calcd. C: 68.03 % H: 8.71 % N: 4.18 % Found C: 67.66 % H: 9.01 % N: 4.28 %
6-3			CDCl ₃ , 300MHz 7.63(1H, dd, J=8.7 Hz) 6.90(1H, d, J=8.7 Hz) 4.36(2H, q, J=7.2 Hz) 4.02(2H, s) 4.00(2H, t, J=6.7 Hz) 3.88(3H, s) 1.6-1.8(2H, m) 1.37 (2H, t, J=7.2 Hz) 1.32(6H, s) 1.3-1.5(4H, m) 0.92(3H, t, J=7.0 Hz)	Neat 2961 173712	FAB+ 364 [M ⁺ H] ⁺ (100) 318(70) 176(50)	

Table 107

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
6-4			CDCl ₃ , 300MHz 7.59(1H, d, J=8.7 Hz) 6.84(1H, d, J=8.7 Hz) 6.66(1H, bs) 4.80(2H, s) 4.09(2H, s) 3.95(2H, t, J=6.7 Hz) 3.88(3H, s) 1.7-1.9(2H, m) 1.39(6H, s) 1.3-1.6(4H, m) 0.94(3H, t, J=7.1 Hz)	Neat 3300 2960 1635 1273	FAB+ 322 [M ⁺ H] ⁺ (100) 304 (80) HRFAB(m/z) Calcd. C ₂₃ H ₃₂ NO ₃ 322.4286 Found 322.2027	
6-5-1			CDCl ₃ , 300MHz 8.06-8.13(1H, m) 7.70(1H, td, J=7.8, 1.7 Hz) 7.61(1H, dd, J=8.4, 1.9 Hz) 7.56(1H, d, J=1.9 Hz) 7.42(1H, d, J=7.8 Hz) 7.21-7.25(1H, m) 6.90(1H, d, J=8.4 Hz) 5.75(1H, dd, J=10.2, 7.2 Hz) 4.13(1H, dd, J=14.8, 7.2 Hz) 4.07(2H, t, J=6.9 Hz) 3.92(3H, s) 1.82-1.92(2H, m)		FAB+ 341 [M ⁺ H] ⁺ (100) 221 (60)	
6-6			7.80(1H, d, J=2.0 Hz), 7.60(1H, dd, J=8.5, 2.0 Hz), 6.83(1H, d, J=8.5 Hz), 4.08(2H, s), 3.93(3H, s), 2.93(2H, t, J=7.3 Hz), 1.3-1.5(10H, m), involving a singlet at 1.37), 0.90(3H, t, J=7.2 Hz).		FAB+ 308[M ⁺ H] ⁺ (100), 292(20).	

Table 108

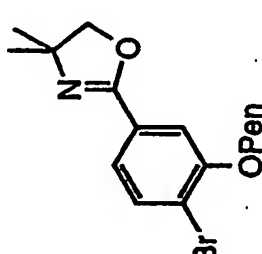
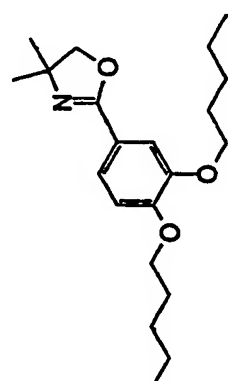
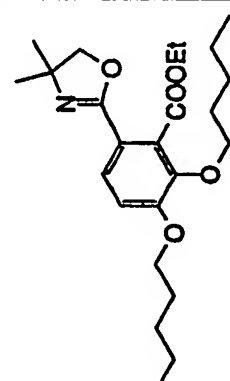
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR, cm ⁻¹	MS	Elem. anal.
6-7	 <p>Colorless oil</p>		CDCl ₃ 300MHz 7.55(1H, d, J=8.1 Hz) 7.44(1H, s) 7.37(1H, d, J=8.1 Hz) 4.13(2H, s) 4.08(2H, t, J=6.6 Hz) 1.80-1.93(2H, m) 1.33-1.60(4H, m) 1.38(6H, s) 0.94(3H, t, J=7.1 Hz)		FAB+ 341[M+H+] (100) 340(100)	
6-8	 <p>Colorless oil</p>		CDCl ₃ 300MHz 7.48(1H, dd, J=8.4, 2.2 Hz), 7.45(2H, d, J=2.2 Hz) 6.85(1H, d, J=8.4 Hz) 4.07(2H, s) 4.0-4.1(4H, m) 1.7-1.9(4H, m) 1.37(6H, m) 1.3-1.6(8H, m) 0.93(3H, t, J=7.1 Hz) 0.93(3H, t, J=7.1 Hz)	Neat 2958 1648 1512	FAB+ 348[M+H+] (100)	
6-9	 <p>Colorless oil</p>		CDCl ₃ 300MHz 7.60(1H, d, J=8.7 Hz) 6.88(1H, d, J=8.7 Hz) 4.36(2H, q, J=7.2 Hz) 4.01(2H, s) 3.9-4.1(4H, m) 1.6-2.0(4H, m) 1.38(3H, t, J=7.2 Hz) 1.32(6H, s) 1.3-1.5(8H, m) 0.8-1.0(6H, m)	Neat 2958 1739 1652 1276	FAB+ 420[M+H+] (100)	

Table 109

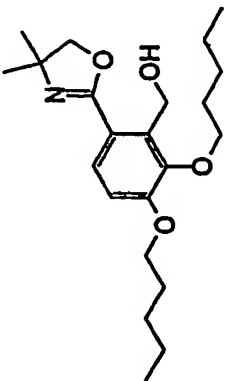
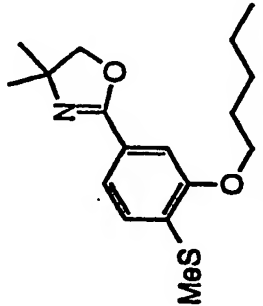
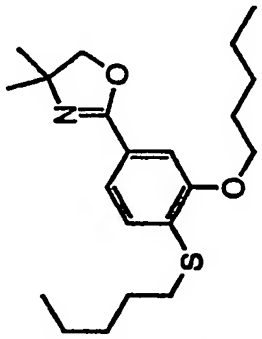
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
6-10	 <p>Colorless oil</p>		CDCl ₃ , 300MHz 7.56(1H, d, J=8.7 Hz) 6.81(1H, d, J=8.7 Hz) 6.64(1H, bs) 4.80(2H, s) 4.07(2H, s) 4.00(2H, t, J=6.5 Hz) 3.95(2H, t, J=6.7 Hz) 1.7-1.9(4H, m) 1.3-1.5(8H, m) 1.38(6H, s)	Neat 3317 2957 1635 1301 1273 1010	FAB+ 378 [M+H] ⁺ (100) 360(80)	
6-11	 <p>Pale-yellow oil</p>		CDCl ₃ , 300MHz 7.50(1H, d, J=8.1 Hz) 7.36(1H, s) 7.08(1H, d, J=8.1 Hz) 4.08(2H, t, J=6.5 Hz) 4.08(2H, s) 2.43(3H, s) 1.80-1.90(2H, m) 1.35-1.50(4H, m) 1.37(6H, s) 0.93(3H, t, J=7.1 Hz)		FAB+ 308[M+H] ⁺ (100)	
6-12	 <p>Pale-yellow oil</p>		CDCl ₃ , 300MHz 7.47(1H, d, J=8.1 Hz), 7.36(1H, s), 7.16(1H, d, J=8.1 Hz), 4.08(2H, s), 4.07(2H, t, J=6.5 Hz), 2.90(2H, t, J=7.4 Hz), 1.80-1.90(2H, m), 1.60-1.75(2H, m), 1.33-1.55(8H, m) 1.37(6H, s) 0.93(3H, t, J=6.9 Hz), 0.90(3H, t, J=6.9 Hz)		FAB+ 364[M+H] ⁺ (100)	

Table 110

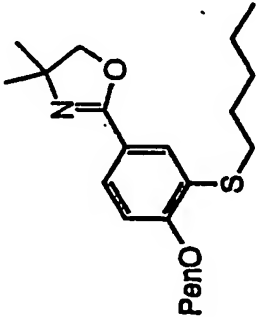
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
6-13	 <p>Colorless oil</p>		CDCl ₃ 300MHz 7.78(1H, d, J = 2.4 Hz), 7.73(1H, dd, J = 8.4, 1.8 Hz), 6.81(1H, d, J = 8.4 Hz), 4.07(2H, s), 4.06(2H, t, J = 6.5 Hz), 2.92(2H, t, J = 7.4 Hz), 1.80-1.90(2H, m), 1.60-1.75(2H, m), 1.33-1.55(14H, m, involving a singlet at 1.37), 0.94(3H, t, J = 6.9 Hz), 0.90(3H, t, J = 6.9 Hz).		FAB+ 364[M+H+] (100), 294(20).	

Table 111

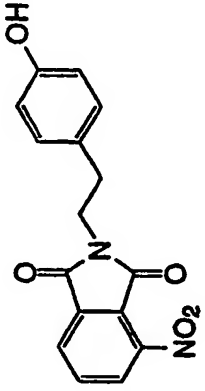
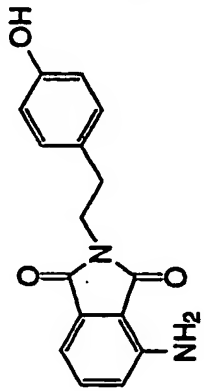
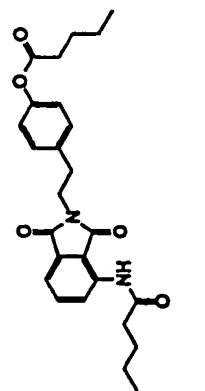
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
7-1		108.2~ 109.2°C	DMSO-d ₆ , 300MHz 9.19(1H, s) 8.26(1H, d, J=7.7 Hz) 8.13(1H, d, J=7.7 Hz) 8.03(1H, d, J=7.7 Hz) 6.99(1H, d, J=8.4 Hz) 6.68(2H, d, J=8.4 Hz) 3.72(2H, t, J=7.5 Hz) 2.78(2H, t, J=7.5 Hz)	KBr 3366 1777 1710	FAB+ 313 [M ⁺ H] ⁺ (20)	
7-2		210.0~ 211.0°C	DMSO-d ₆ , 300MHz 9.16(1H, s) 7.39(1H, dd, J=7.0 Hz) 6.39(2H, d, J=8.4 Hz) 6.94(1H, d, J=8.3 Hz) 6.91(1H, d, J=8.3 Hz) 6.63(2H, d, J=8.4 Hz) 6.40(2H, br) 3.65(2H, t, J=7.3 Hz) 2.75(2H, t, J=7.3 Hz)	KBr 3382 3254 2942 1744 1673	FAB+ 283 [M ⁺ H] ⁺ (40)	
7-3		119.0~ 120.2°C	CDCl ₃ , 300MHz 9.5(1H, s) 8.8(1H, d, J=6 Hz) 7.6(1H, t, J=6 Hz) 7.5(2H, d, J=6 Hz) 7.2(2H, d, J=9 Hz) 7.0(2H, d, J=9 Hz) 3.9(2H, t, J=7.5 Hz) 3.0(2H, t, J=7.5 Hz) 2.5(2H, t, J=7.5 Hz) 2.5(2H, t, J=7.5 Hz) 1.6-1.8(4H, m) 1.4-1.6(4H, m)	KBr 3479 3372 1739 1692 1633	FAB+ 451 [M ⁺ H] ⁺ (30) 367(20)	

Table 112

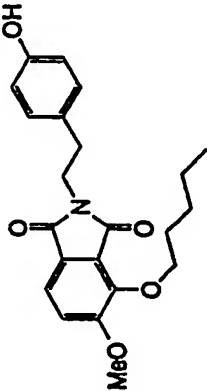
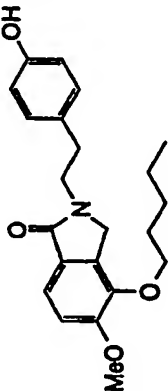
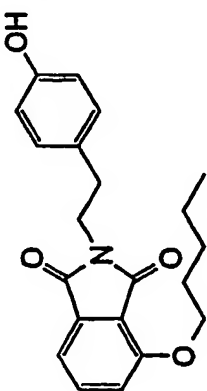
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-4			DMSO-d ₆ 300MHz 7.50(1H, d, J=8.0 Hz) 7.09(2H, d, J=8.3 Hz) 7.07(1H, d, J=8.0 Hz) 6.74(2H, d, J=8.3 Hz) 5.40(1H, bs) 4.26(2H, t, J=6.8 Hz) 3.92(3H, s) 3.83(2H, t, J=7.7 Hz) 2.89(2H, t, J=7.7 Hz) 1.7-1.9(2H, m) 1.3-1.5(4H, m) 0.92(3H, t, J=7.2 Hz)			
7-5		146.3 ~ 146.9 °C	CDCl ₃ 300MHz 7.52(1H, d, J=8.3 Hz) 7.06(2H, d, J=8.4 Hz) 6.97(1H, d, J=8.3 Hz) 6.75(2H, d, J=8.4 Hz) 6.40(1H, bs) 4.24(2H, s) 4.03(2H, t, J=6.7 Hz) 3.89(3H, s) 3.82(2H, t, J=7.2 Hz) 2.91(2H, t, J=7.2 Hz) 1.6-1.8(2H, m) 1.3-1.5(4H, m)	KBr 3129 2936 1639 1273	FAB+ 370 [M ⁺ H] ⁺ (100) 262(40)	C ₂₂ H ₂₇ NO ₄ Calcd. C; 71.52% H; 7.37% N; 3.79% Found C; 71.50% H; 7.39% N; 3.87%
7-6			CDCl ₃ 300MHz 7.61(1H, t, J=7.83 Hz) 7.38(1H, d, J=7.22 Hz) 7.16(1H, d, J=8.43 Hz) 7.11(2H, d, J=8.30 Hz) 6.75(2H, d, J=8.33 Hz) 4.5-4.8(1H, br) 4.16(2H, t, J=6.64 Hz) 3.84(2H, t, J=7.69 Hz) 2.90 (2H, t, J=7.68 Hz) 1.84-1.92(2H, m) 1.35-1.52(4H, m) 0.94(3H, t, J=7.04 Hz)	Neat 3422 3021 2955 2871 1766 1704 1614 1516		

Table 113

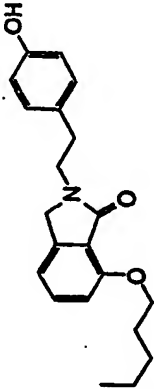
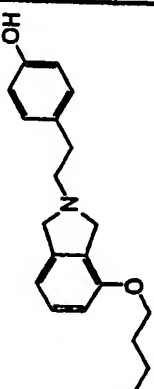
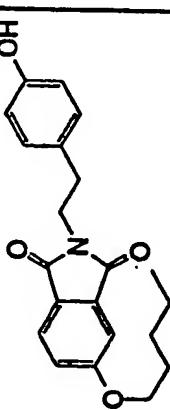
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-7		161.3 ~ 161.6°C	CDCl ₃ , 300MHz 7.39(1H, t, J=7.90 Hz) 7.04(2H, d, J=7.50 Hz) 6.89(1H, d, J=7.40 Hz) 6.85(1H, d, J=8.10 Hz) 6.80(2H, d, J=8.50 Hz) 4.14(2H, s) 4.07(2H, t, J=6.75 Hz) 3.76(2H, t, J=7.15 Hz) 2.87(2H, t, J=7.15 Hz) 1.88(2H, quint, J=7.15 Hz) 1.30-1.51(4H, m) 0.90(3H, t, J=7.15 Hz)	Neat 3163 2950 2868 1662 1612 1596	FAB+ 340 [M ⁺ H] ⁺ (100) 326(60) 270(18)	
7-8		107.8 ~ 108.1°C	CDCl ₃ , 300MHz 7.26(1H, t, J=7.76 Hz) 7.07(2H, d, J=8.47 Hz) 6.79(1H, d, J=7.44 Hz) 6.69(1H, d, J=8.07 Hz) 6.67(2H, d, J=8.45 Hz) 4.02(4H, s) 3.97(2H, t, J=6.54 Hz) 2.80-3.00(4H, m) 1.70-1.85(2H, m) 1.30-1.45(4H, m) 0.93(3H, t, J=7.01 Hz)	Neat 3400 2943 2870 2806 1613 1594	FAB+ 326 [M ⁺ H] ⁺ (100) 218(62) 121(20)	
7-9		114.7 ~ 115.1°C	CDCl ₃ , 300MHz 7.69(1H, d, J=8.25 Hz) 7.26(1H, d, J=2.19 Hz) 7.05-1.12(3H, m) 6.73(2H, d, J=8.46 Hz) 5.83 (1H, s) 4.03(2H, t, J=6.54 Hz) 3.85(2H, t, J=7.52 Hz) 2.89(2H, t, J=7.49 Hz) 1.75-1.84(2H, m) 1.32-1.47(4H, m) 0.93(3H, t, J=7.01 Hz)	Neat 3435 2934 1765 1696 1613 1515	FAB+ 354 [M ⁺ H] ⁺ (100) 289(16) 246(20)	C ₂₁ H ₂₃ NO ₄ Calcd. C: 71.37% H: 6.56% N: 3.96% Found C: 71.39% H: 6.62% N: 3.99%

Table 114

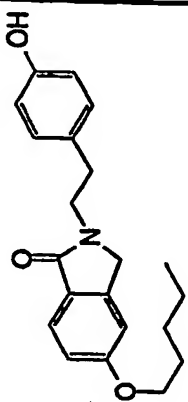
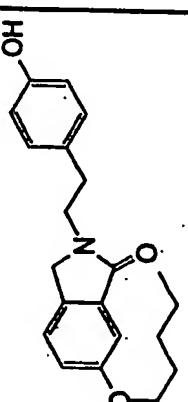
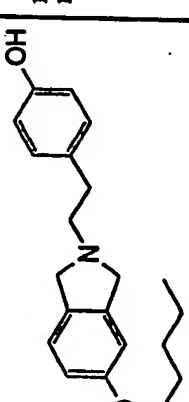
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
7-10-1		138.5 ~ 138.8 °C	CDCl ₃ , 300MHz 7.72(1H, d, J=8.42 Hz) 7.04(2H, d, J=8.50 Hz) 6.93(1H, dd, J=8.44, 2.17 Hz) 6.85(1H, d, J=1.73 Hz) 6.76(2H, d, J=6.48 Hz) 3.98(2H, t, J=6.53 Hz) 3.83(2H, t, J=7.09 Hz) 2.90(2H, t, J=7.07 Hz) 1.77-1.82(2H, m) 1.37-1.45(4H, m) 0.93(3H, t, J=7.06 Hz)	Neat 3132 3012 2953 2867 1738 1662 1617 1594	FAB+ 340 [M ⁺ H] ⁺ (100) 324(28) 232(33)	
7-10-2		137.5 ~ 137.8 °C	CDCl ₃ , 300MHz 7.31(1H, d, J=2.33 Hz) 7.24(1H, d, J=7.89 Hz) 7.03-7.08(3H, m) 6.76(2H, d, J=8.48 Hz) 6.24(1H, br) 3.97(2H, t, J=6.59 Hz) 3.84(2H, t, J=7.19 Hz) 2.91(2H, t, J=7.16 Hz) 1.75-1.81(2H, m) 1.38-1.42(4H, m) 0.93(3H, t, J=7.03 Hz)	Neat 3103 2934 1654 1618 1594	FAB+ 340 [M ⁺ H] ⁺ (100) 324(25) 232(32)	
7-11		120.5 ~ 120.7 °C	CDCl ₃ , 300MHz 7.04-7.09(3H, m) 6.64-6.75(4H, m) 3.90-3.96 (6H, m) 2.80-2.97(4H, m) 1.74-1.79(2H, m) 1.36-1.44(4H, m) 0.93(3H, t, J=7.04 Hz)	Neat 2941 2873 2807 1612 1590	FAB+ 326 [M ⁺ H] ⁺ (97) 218(100) 191(26) 121(78)	C ₂₄ H ₂₇ NO ₃ Calcd. C: 77.50% H: 8.36% N: 4.30% Found C: 77.29% H: 8.56% N: 4.29%

Table 115

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ⁻¹	MS	Elem. anal.
7-13			CDCl ₃ , 300MHz 7.38(1H, d, J=8.4 Hz) 7.3-7.5(5H, m) 7.13(2H, d, J=8.6 Hz) 6.91(1H, d, J=8.4 Hz) 6.88(2H, d, J=8.6 Hz) 5.64(1H, d, J=9.8 Hz) 5.01(2H, s) 4.0-4.2(2H, m) 3.86(3H, s) 3.7-3.8(1H, m) 3.5-3.6(1H, m) 2.97(2H, d, J=9.8 Hz)	Neat 3300 2933 1670 1268	FAB+ 476 [M ⁺ H] ⁺ (50) 458(60)	C ₂₀ H ₂₃ NO ₃ Calcd. C: 73.24% H: 6.99% N: 2.95% Found C: 73.06% H: 7.06% N: 2.81 %
7-14			CDCl ₃ , 300MHz 7.53(1H, d, J=8.2 Hz) 7.3-7.5(5H, m) 7.15(2H, d, J=8.6 Hz) 6.99(1H, d, J=8.2 Hz) 6.90(2H, d, J=8.6 Hz) 5.02(2H, s) 4.20(2H, s) 4.03(2H, d, J=6.7 Hz) 3.90(3H, s) 3.80(2H, t, J=7.4 Hz) 3.80(2H, t, J=7.4 Hz) 2.92(2H, t, J=7.4 Hz)		FAB+ 460 [M ⁺ H] ⁺ (100) 262(50)	
7-17		106.3 ~ 107.2 °C	CDCl ₃ , 300MHz 8.20(1H, d, J=9.1 Hz) 7.3-7.5(5H, m) 7.13(1H, d, J=9.1 Hz) 7.12(2H, d, J=8.6 Hz) 6.90(2H, d, J=8.6 Hz) 6.77(1H, d, J=7.7 Hz) 6.65(1H, d, J=7.7 Hz) 5.04(2H, s) 4.13(2H, t, J=7.4 Hz) 4.01(2H, t, J=6.7 Hz) 3.96(3H, s) 3.01(2H, t, J=7.3 Hz)	KBr 3438 2950 1652 1623 1597 1510 1283 1085	FAB+ 472 [M ⁺ H] ⁺ (100)	C ₂₀ H ₂₃ NO ₄ Calcd. C: 76.41% H: 7.05% N: 2.97% Found C: 76.55% H: 7.06% N: 2.96 %

Table 116

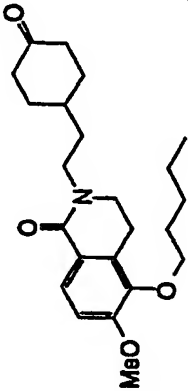
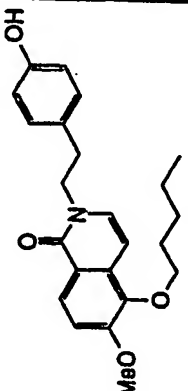
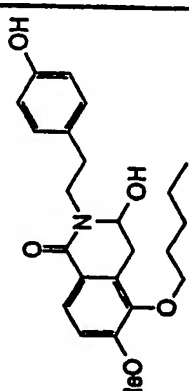
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR _{cm⁻¹}	MS	Elem. anal.
7-18			CDCl ₃ , 300MHz 7.83(1H, d, J=8.5 Hz) 6.88(1H, d, J=8.5 Hz) 3.93(2H, t, J=6.6 Hz) 3.89(3H, s) 3.63(2H, t, J=7.4 Hz) 3.54(2H, t, J=6.6 Hz) 3.02(2H, t, J=6.6 Hz) 2.3-2.4 (4H, m) 2.1-2.2(2H, m) 1.5-1.9(5H, m) 1.3-1.5 (6H, m) 0.94(3H, t, J=7.2 Hz)	Neat 2954 1714 1644 1279	FAB+ 388[M+H+] (100)	
7-19-1		130.3 ~ 131.1 °C	CDCl ₃ , 300MHz 8.20(1H, d, J=8.9 Hz) 7.13(1H, d, J=8.9 Hz) 7.08(1H, bs) 7.02(2H, d, J=8.2 Hz) 6.85(1H, d, J=7.5 Hz) 6.82(2H, d, J=8.2 Hz) 6.72(1H, d, J=7.5 Hz) 4.15(2H, t, J=7.5 Hz) 4.01(2H, t, J=6.7 Hz) 3.95(3H, s) 2.98(2H, t, J=7.5 Hz) 1.7-1.9(2H, m)	Neat 3250 2959 1642 1586 1514 1283	FAB+ 381 [M+H] ⁺ (100) 261(40) 191(40)	C ₂₀ H ₂₇ NO ₂ Calcd. C: 72.42% H: 7.13% N: 3.66% Found C: 72.30% H: 7.21% N: 3.58%
7-19-2						

Table 117

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-20		90.2~ 90.3°C	CDCl ₃ , 300MHz 8.51(2H, d, J=5.9 Hz) 8.19(1H, d, J=8.9 Hz) 7.14(1H, d, J=8.9 Hz) 7.14(2H, d, J=5.9 Hz) 6.76(1H, d, J=7.6 Hz) 6.67(1H, d, J=7.6 Hz) 4.19(2H, t, J=7.3 Hz) 4.01(2H, t, J=6.7 Hz) 3.97(3H, s) 3.09(2H, t, J=7.3 Hz) 1.7-1.9(2H, m) 1.3-1.5(4H, m)	Neat 3478 2936 1650 1625 1596 1484 1284	FAB+ 367 [M ⁺ H] ⁺ (50)	C ₂₂ H ₂₀ N ₂ O ₃ Calcd. C: 72.11% H: 7.15% N: 7.64% Found C: 72.03% H: 7.25% N: 7.54%
7-22			CDCl ₃ , 300MHz 8.20(1H, d, J=8.9 Hz) 7.22(2H, d, J=8.5 Hz) 7.14(1H, d, J=8.9 Hz) 7.01(2H, d, J=8.5 Hz) 6.80(1H, d, J=7.6 Hz) 6.67(1H, d, J=7.6 Hz) 4.15(2H, t, J=7.5 Hz) 4.01(2H, t, J=6.7 Hz) 3.96(3H, s) 3.07(2H, t, J=7.5 Hz) 2.29(3H, s) 1.7-1.9(2H, m)	KBr 3438 2957 1762 1654 1627 1283	FAB+ 424 [M ⁺ H] ⁺ (50)	C ₂₃ H ₂₀ N ₂ O ₄ Calcd. C: 70.90% H: 6.90% N: 3.31% Found C: 71.10% H: 6.99% N: 3.22%
7-23			CDCl ₃ , 300MHz 7.84(1H, d, J=8.6 Hz) 7.27(2H, d, J=8.4 Hz) 7.01(2H, d, J=8.4 Hz) 6.87(1H, d, J=8.6 Hz) 3.90(2H, t, J=6.7 Hz) 3.88(3H, s) 3.75(2H, t, J=7.5 Hz) 3.38(2H, t, J=6.6 Hz) 2.95(2H, t, J=7.5 Hz) 2.89(2H, t, J=6.6 Hz) 2.28(3H, s) 1.7-1.8(2H, m)	KBr 2936 1756 1646 1219	FAB+ 426 [M ⁺ H] ⁺ (100) 276(50)	

Table 118

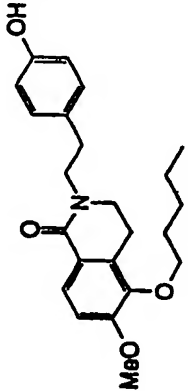
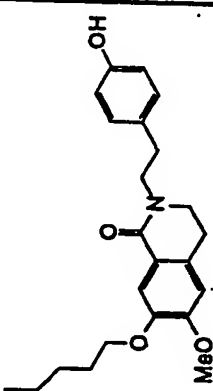
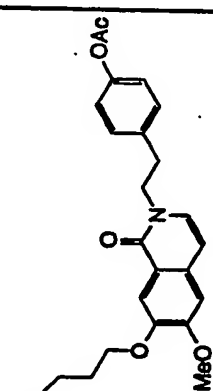
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-24		143.6~ 144.4°C	CDCl ₃ , 300MHz 7.82(1H, d, J=8.6 Hz) 7.08(2H, d, J=8.4 Hz) 6.85(1H, d, J=8.6 Hz) 6.79(2H, d, J=8.4 Hz) 6.35(1H, s) 3.90(2H, t, J=6.7 Hz) 3.87(3H, s) 3.73(2H, t, J=7.1 Hz) 3.59(2H, t, J=6.6 Hz) 2.90(2H, t, J=6.6 Hz) 2.86(2H, t, J=7.1 Hz) 1.6-1.8(2H, m)		FAB+ 384 [M ⁺ H] ⁺ (100) 276(60) 264(40)	C ₂₃ H ₂₉ NO ₄ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 72.04% H: 7.79% N: 3.55%
7-25		170.6~ 171.4°C	CDCl ₃ , 300MHz 7.59(1H, s) 7.10(2H, d, J=8.5 Hz) 7.00(1H, br s) 6.77(2H, d, J=8.5 Hz) 6.58(1H, s) 4.02(2H, t, J=6.9 Hz) 3.88(3H, s) 3.73(2H, t, J=7.3 Hz) 3.39(2H, t, J=6.7 Hz) 2.87(2H, t, J=7.3 Hz) 2.77(2H, t, J=6.7 Hz) 1.8-1.9(2H, m)	Neat 3227 2934 2361 1600 1516 1280	FAB+ 384 [M ⁺ H] ⁺ (40)	C ₂₃ H ₂₉ NO ₄ Calcd. C: 72.04% H: 7.62% N: 3.65% Found C: 71.93% H: 7.65% N: 1113.62
7-26			CDCl ₃ , 300MHz 7.82(1H, s) 7.21(2H, d, J=8.5 Hz) 7.00(2H, d, J=8.5 Hz) 6.83(1H, s) 6.74(1H, d, J=7.3 Hz) 6.31(1H, d, J=7.3 Hz) 4.19 2H, t, J=7.3 Hz) 4.10(2H, t, J=6.9 Hz) 4.00(3H, s) 3.08(2H, t, J=7.3 Hz) 2.29(3H, s) 1.8-2.0(2H, m)		FAB+ 424 [M ⁺ H] ⁺ (100) 261(70)	

Table 119

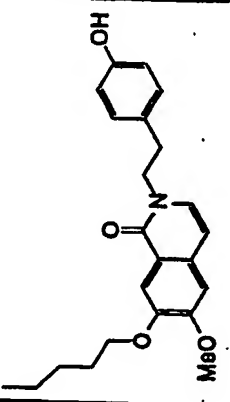
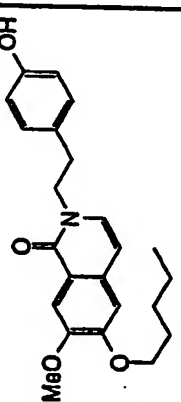
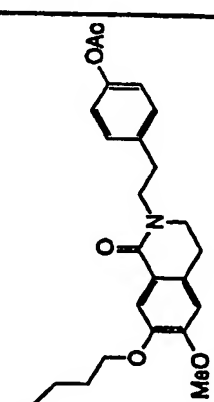
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-27		209.4 ~ 210.7 °C	DMSO-d ₆ , 300 MHz 9.2(1H, bs) 7.6(1H, s) 7.2(1H, d, J=6 Hz) 7.1(1H, s) 7.0(2H, d, J=9 Hz) 6.6(2H, d, J=9 Hz) 6.4(1H, d, J=6 Hz) 4.0-4.1(2H, m) 4.0(2H, t, J=6 Hz) 3.9(3H, s) 2.8(2H, t, J=8 Hz) 1.7-1.8(2H, m)	KBr 3441 2953 1565 1516	FAB+ 382 [M+H] ⁺ (100) 261(50)	
7-28		147.2 ~ 148.3 °C	DMSO-d ₆ , 300 MHz 9.2(1H, bs) 7.6(1H, s) 7.2(1H, d, J=6 Hz) 7.1(1H, s) 7.0(2H, d, J=9 Hz) 6.6(2H, d, J=9 Hz) 6.4(1H, d, J=6 Hz) 4.0-4.1(2H, m) 4.0(2H, t, J=6 Hz) 3.9(3H, s) 2.8(2H, t, J=8 Hz) 1.7-1.8(2H, m)	KBr 3441 2953 1565 1516	FAB+ 382 [M+H] ⁺ (100) 261(50)	
7-29		93.2 ~ 94.1 °C	CDCl ₃ , 300 MHz 7.60(1H, s) 7.27(2H, d, J=8.5 Hz) 7.01(2H, d, J=8.5 Hz) 6.59(1H, s) 4.02(2H, t, J=6.9 Hz) 3.90(3H, s) 3.75(2H, t, J=7.3 Hz) 3.38(2H, t, J=6.7 Hz) 2.95(2H, t, J=7.3 Hz) 2.77(2H, t, J=6.7 Hz) 2.28(3H, s) 1.8-1.9(2H, m)	Neat 13-1.5(4H, m) 0.93(3H, t, J=7.0 Hz)	FAB+ 426 [M+H] ⁺ (60) 276(55) HRPAB(m/z) Calcd. C ₂₃ H ₂₁ NO ₃ 426.5380 Found 426.2277	C ₂₃ H ₂₁ NO ₃ Calcd. C: 70.57% H: 7.34% N: 3.29% Found C: 70.19% H: 7.36% N: 3.24 %

Table 120

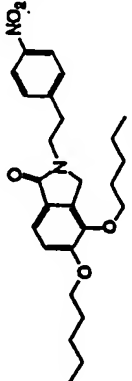
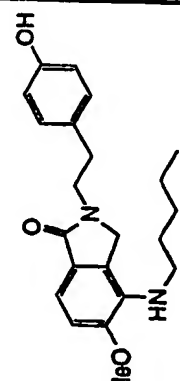
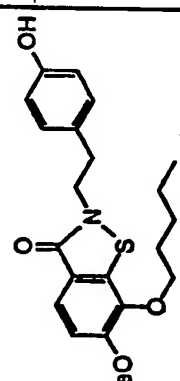
Ex:	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-30		96.2-96.7 °C	CDCl ₃ , 300MHz 8.15(2H, d, J=8.7 Hz) 7.49(1H, d, J=8.3 Hz) 7.42(2H, d, J=8.7 Hz) 6.99(1H, d, J=8.3 Hz) 4.22(2H, s) 4.06(2H, t, J=6.7 Hz) 4.04(2H, t, J=6.5 Hz) 3.88(2H, t, J=7.2 Hz) 3.11(2H, t, J=7.2 Hz) 1.8-1.9(2H, m) 1.7-1.8(2H, m) 1.3-1.5(8H, m)	KBr 2933 1687 1516 1344	FAB+ 455 [M+H+] (100), 318 (100)	C ₂₆ H ₃₄ N ₂ O ₅ Calcd. C: 68.70% H: 7.54% N: 6.16% Found C: 68.92% H: 7.54% N: 6.05%
7-31		115.0~ 116.5°C	CDCl ₃ , 300MHz 7.27(1H, d, J=8.2 Hz) 7.10(2H, d, J=8.4 Hz) 6.84(1H, d, J=8.2 Hz) 6.69(2H, d, J=8.4 Hz) 5.38(2H, s) 3.88(3H, s) 3.70(2H, t, J=7.7 Hz) 3.14(2H, t, J=7.1 Hz) 2.89(2H, t, J=7.7 Hz) 1.5-1.63(2H, m) 1.3-1.4(4H, m) 0.91(3H, t, J=8.0 Hz)	KBr 2932 1676 1515 1261	FAB+ 369 [M+H+] (100) 261(50)	
7-32		110.0- 111.0°C	CDCl ₃ , 300MHz 7.71(1H, d, J=8.4 Hz) 7.39(1H, bs) 7.05(2H, d, J=8.1 Hz) 7.00(1H, d, J=8.4 Hz) 6.76(2H, d, J=8.1 Hz) 4.13(2H, t, J=6.6 Hz) 4.07(2H, t, J=7.4 Hz) 3.93(3H, s) 2.97(2H, t, J=7.4 Hz) 1.65-1.8(2H, m) 1.3-1.5(4H, m) 0.94(3H, t, J=7.1 Hz)		FAB+ 388[M+H+] (100) 267(50)	C ₂₁ H ₂₅ N ₂ O ₄ S

Table 121

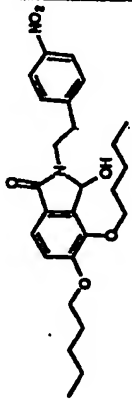
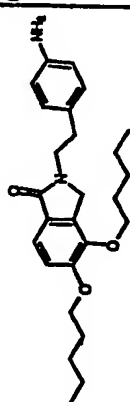
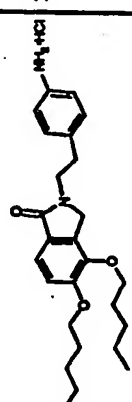
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-33			CDCl ₃ , 300MHz 8.12(2H, d, J=8.6 Hz) 7.90(1H, d, J=8.6 Hz) 7.31(1H, d, J=8.2 Hz) 6.89(1H, d, J=8.2 Hz) 5.69(2H, d, J=9.6 Hz) 4.0-4.2(2H, m) 3.98(2H, t, J=6.5 Hz) 3.7-3.9(1H, m) 3.6-3.8(1H, m) 3.2-3.3(1H, m) 3.08(2H, q, J=7.0 Hz) 1.7-1.9(4H, m)	Neat 3300 2960 1673 1520 1345 1269	FAB+ 471 [M+H] ⁺ (20), 453(60), 165(100).	
7-34		67.2-67.8 °C	CDCl ₃ , 300MHz 7.46(1H, d, J=8.2 Hz) 7.02(2H, d, J=8.3 Hz) 6.97(1H, d, J=8.2 Hz) 6.61(2H, d, J=8.3 Hz) 4.20(2H, s) 4.05(2H, t, J=6.6 Hz) 4.03(2H, t, J=6.5 Hz), 3.76(2H, t, J=7.4 Hz) 3.58(2H, br), 2.86(2H, t, J=7.4 Hz) 1.8-1.9(2H, m) 1.7-1.8(2H, m)	Neat 3346 2931 1681 1620 1272	FAB+ 425 [M+H] ⁺ (65), 120(100)	C ₂₆ H ₃₆ N ₂ O ₃ Calcd. C: 73.55% H: 8.55% N: 6.60% Found C: 73.39% H: 8.74% N: 6.47%
7-35		213.6- 214.6 °C	DMSO-d ₆ , 300MHz 10.19(3H, br) 7.34(1H, d, J=8.4 Hz) 7.28(2H, d, J=8.4 Hz) 7.26(2H, d, J=8.4 Hz) 7.06(1H, d, J=8.4 Hz) 4.40(2H, s) 4.03(4H, t, J=6.6 Hz) 3.70(2H, t, J=7.2 Hz) 2.93(2H, t, J=7.2 Hz) 1.6-1.8(4H, m) 1.2-1.5(8H, m) 0.89(6H, t, J=7.2 Hz)	KBr	FAB+ 425[M+H] ⁺ (100)	C ₂₆ H ₃₆ N ₂ O ₃ · HCl Calcd. C: 50.00% H: 10.00% N: 5.00%

Table 122

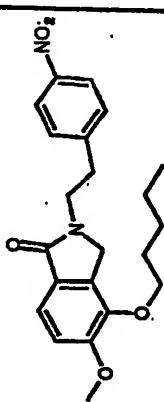
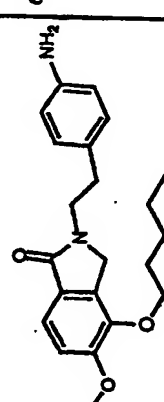
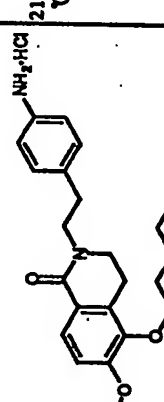
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-36			CDCl ₃ 300MHz 8.15(2H, d, J=8.4 Hz) 7.52(1H, d, J=8.4 Hz) 7.41(2H, d, J=8.4 Hz), 7.00(1H, d, J=8.4 Hz) 4.23(2H, s), 4.04(2H, t, J=6.6 Hz) 3.90(3H, s) 3.88(2H, t, J=7.5 Hz) 3.11(2H, t, J=7.5 Hz) 1.7-1.8(2H, m) 1.3-1.5(8H, m) 0.92(3H, t, J=6.9 Hz)		FAB+ 399[M+H+] (100), 262(80)	
7-37		64-67 °C	CDCl ₃ 300MHz 7.52(1H, d, J=8.4 Hz) 7.02(2H, d, J=8.4 Hz) 6.98(1H, d, J=8.4 Hz) 6.61(2H, d, J=8.4 Hz) 4.20(2H, s) 4.02(2H, t, J=6.6 Hz) 3.90(3H, s) 3.76(2H, t, J=6.9 Hz) 3.30(2H, bs) 2.86(1H, d, J=6.9 Hz) 1.7-1.9(2H, m) 1.3-1.5(4H, m)	KBr 3348 2931 1682 1621 1518 1272	FAB+ 369[M+H+] (100)	
7-38		212~215 °C(dec.)	CDCl ₃ 300MHz 10.46(3H, bs) 7.71(1H, d, J=8.4 Hz) 7.49(2H, d, J=8.4 Hz) 7.26(2H, d, J=8.4 Hz) 6.82(1H, d, J=6.0 Hz) 3.89(2H, d, J=6.6 Hz) 3.85(3H, s) 3.71(2H, t, J=7.5 Hz) 3.44(2H, t, J=6.0 Hz) 2.92(4H, qu, J=6.6 Hz) 1.7-1.8(2H, m) 1.3-1.5(4H, m)		FAB+ 383 [M+H+](50), 120(100)	

Table 123

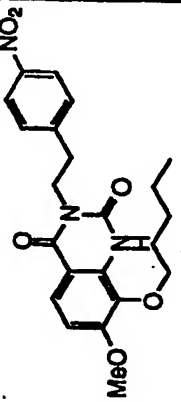
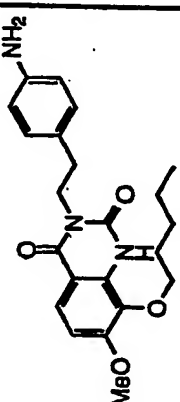
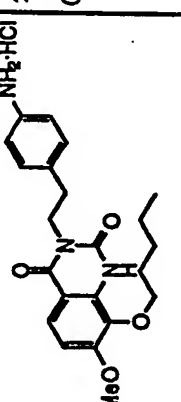
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-39			DMSO-d ₆ 300MHz 10.7(1H,s) 8.14(2H,d,J=8.4Hz) 7.66(1H,d,J=8.7Hz) 7.50(2H,d,J=8.4Hz) 6.97(1H,d,J=8.7Hz) 4.15(2H,t,J=7.4Hz) 3.91(2H,t,J=6.9Hz) 3.88(3H,s) 3.03(2H,t,J=7.1Hz) 1.70-1.80(2H,m) 1.30-1.45(4H,m) 0.88(3H,t,J=7.1Hz)			
7-40		154.9~ 155.7°C	CDCl ₃ 300MHz 8.05(1H,s) 7.83(1H,d,J=9.0Hz) 7.12(2H,d,J=7.8Hz) 6.80(1H,d,J=9.0Hz) 6.64(2H,d,J=7.8Hz) 4.18(2H,t,J=8.0Hz) 4.08(2H,t,J=7.1Hz) 3.95(3H,s) 3.58(2H,bs) 2.86(2H,t,J=8.1Hz) 1.73-1.85(2H,m) 1.30-1.50(4H,m)	KBr 2954 1708 1654 1618	PAB+ 398 [M+H+] ⁺ (30)	
7-41		244-249 °C (decomp)	DMSO-d ₆ 300MHz 10.73(1H,s) 10.17(2H,bs) 7.66(1H,d,J=8.7Hz) 7.32(2H,d,J=8.7Hz) 7.28(2H,d,J=8.7Hz) 6.96(1H,d,J=8.7Hz) 4.08(2H,t,J=7.5Hz) 3.91(2H,t,J=7.4Hz) 3.88(3H,s) 3.44(2H,bs) 2.88(2H,t,J=7.5Hz) 1.66-1.80(2H,m)	KBr 2953 2542 1705 1665 1621 1412	PAB- 396(20) 326(20)	C ₂₂ H ₂₈ N ₂ O ₄ Calcd. C: 60.89% H: 6.50% N: 9.68% Found C: 60.95% H: 6.56% N: 9.63%

Table 124

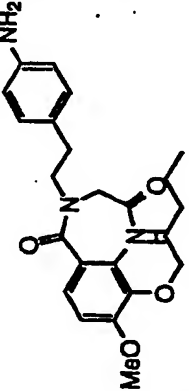
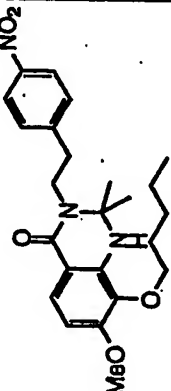
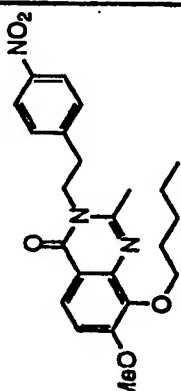
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elen. anal.
7-42		161.0~ 164.0°C	DMSO-d6, 300MHz 9.43(1H,s) 7.46(1H,d,J=9.0Hz) 6.97(2H,d,J=9.0Hz) 6.88(2H,d,J=8.1Hz) 6.47(2H,d,J=8.1Hz) 4.87(2H,s) 3.90(2H,t,J=6.6Hz) 3.84(3H,s) 3.78(2H,bs) 3.62(2H,t,J=7.7Hz) 2.64(2H,t,J=7.7Hz) 1.60-1.75(2H,m)	KBr 3455 3360 2935 1694 1634 1465 1290	FAB+ 412 [M+H+](50)	C23H29N3O4
7-43						
7-44						

Table 125

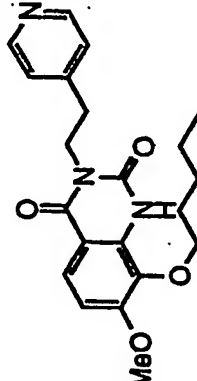
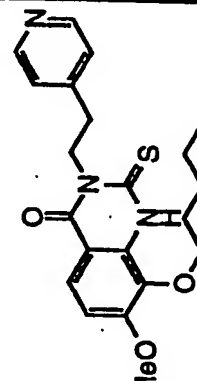
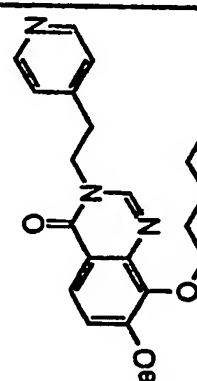
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
7-45		210.1~ 212.3 °C	DMSO-d ₆ 300MHz 10.81(1H,s) 8.78(2H,d,J=6.5Hz) 7.89(2H,d,J=6.5Hz) 7.65(1H,d,J=8.9Hz) 6.98(1H,d,J=8.9Hz) 4.24(2H,t,J=6.9Hz) 3.91(2H,t,J=6.2Hz) 3.89(3H,s) 3.18(2H,t,J=6.9Hz) 1.70-1.80(2H,m) 1.23-1.40(4H,m) 0.89(3H,t,J=7.04Hz)	KBr 2933 1714 1672 1616 1370 1296	FAB+ 384[M+H] ⁺ (100) 238(20)	C ₂₁ H ₂₅ N ₃ O ₄
7-46		107.5~ 108.5 °C	CDCl ₃ 300MHz 9.51(1H,s) 8.54(2H,d,J=6.0Hz) 7.82(1H,d,J=9.0Hz) 7.32(2H,d,J=6.0Hz) 6.91(1H,d,J=9.0Hz) 4.71(2H,t,J=8.3Hz) 4.14(2H,t,J=7.1Hz) 3.97(3H,s) 3.10(2H,t,J=8.1Hz) 1.75-1.90(2H,m) 1.30-1.50(4H,m) 0.96(3H,t,J=7.1Hz)	KBr 3415 2952 2363 1687 1620 1488 1144 1094	FAB+ 400 [M+H] ⁺ (20)	C ₂₁ H ₂₅ N ₃ O ₃ S
7-47			CDCl ₃ 300MHz 8.54(2H,d,J=5.9Hz) 8.08(1H,d,J=9.0Hz) 7.75(1H,s) 7.18(1H,d,J=9.0Hz) 7.14(2H,d,J=6.9Hz) 4.21(2H,t,J=7.2Hz) 4.14(2H,t,J=7.0Hz) 3.99(3H,s) 3.12(2H,t,J=7.3Hz) 1.75-1.90(2H,m) 1.30-1.50(4H,m) 0.92(3H,t,J=7.1Hz)			

Table 126

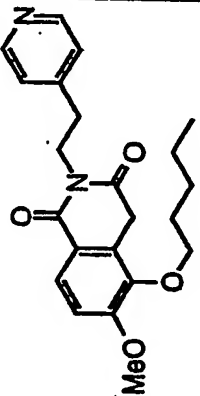
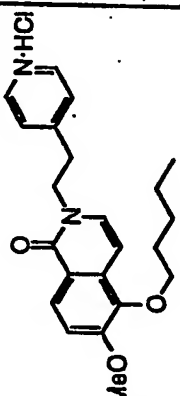
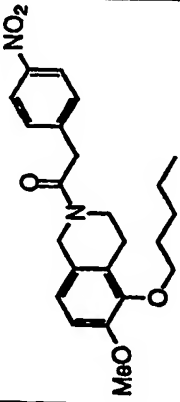
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR ^{cm-1}	MS	Elem. anal.
7-48			DMSO-d ₆ 300MHz 8.79(2H,d,J=6.0Hz) 7.95(2H,d,J=6.0Hz) 7.76(1H,d,J=8.7Hz) 7.18(1H,d,J=8.7Hz) 4.18(2H,t,J=6.9Hz) 3.91(2H,t,J=7.7Hz) 3.91(2H,s) 3.88(3H,s) 3.14(2H,t,J=6.8Hz) 1.60-1.78(2H,m) 1.25-1.50(4H,m) 0.90(3H,t,J=7.1Hz)			
7-49		152.8 ~ 153.3 °C	DMSO-d ₆ 300MHz 8.81(2H,d,J=6.6Hz) 7.95(1H,d,J=9.0Hz) 7.92(2H,d,J=6.6Hz) 7.38(1H,d,J=7.5Hz) 7.30(1H,d,J=9.0Hz) 6.51(1H,d,J=7.5Hz) 4.30(2H,t,J=6.9Hz) 3.95(2H,t,J=6.6Hz) 3.91(3H,s) 3.31(2H,t,J=7.2Hz) 1.65-1.77(2H,m) 1.28-1.49(4H,m)	KBr 3436 2389 1655 1630 1285 1087		C ₂₂ H ₂₇ ClN ₂ O ₃ Calcd. C: 65.58% H: 6.75% N: 6.95% Found C: 65.34% H: 6.89% N: 6.98%
7-50						

Table 127

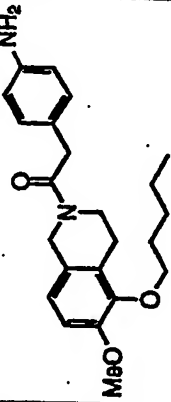
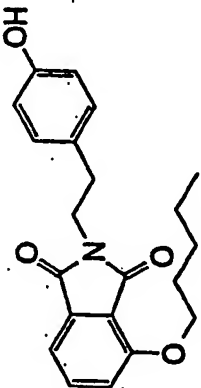
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
7-51	 <p>Colorless oil</p>		DMSO-d ₆ , 300MHz 6.77-6.93(4H, m) 6.51(2H, d, J=8.4Hz) 4.52(2H, s) 4.51(2H, bs) 3.88(2H, t, J=6.5Hz) 3.75(3H, s) 3.63(2H, t, J=6.0Hz) 3.56(2H, s) 2.68(2H, t, J=5.9Hz) 1.60-1.73(2H, m) 1.30-1.50(4H, m) 0.89(3H, t, J=7.2Hz)		FAB+ 383 [M+H] ⁺ (80) 289(50)	C ₂₃ H ₃₀ N ₂ O ₃
7-52	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.61(1H, t, J=7.83 Hz) 7.38(1H, d, J=7.22 Hz) 7.16(1H, d, J=8.43 Hz) 7.11(2H, d, J=8.30 Hz) 6.75(2H, d, J=8.33 Hz) 4.5-4.8(1H, br) 4.16(2H, t, J=6.64 Hz) 3.84(2H, t, J=7.69 Hz) 2.90(2H, t, J=7.68 Hz) 1.84-1.92(2H, m) 1.35-1.52(4H, m) 0.94(3H, t, J=7.04 Hz)	Neat 3422 3021 2953 2871 1766 1704 1614 1516		

Table 128

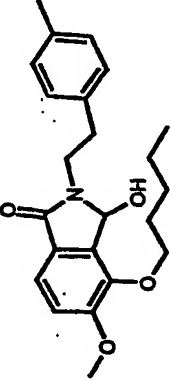
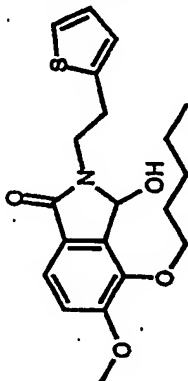
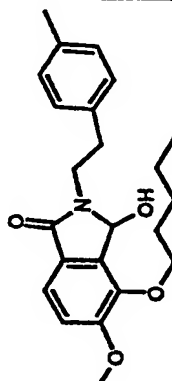
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-54	 <p>Pale-yellow crystals</p>		CDCl ₃ , 300MHz 8.12(2H, d, J=8.7 Hz) 7.39(2H, d, J=8.7 Hz) 7.33(1H, d, J=8.1 Hz) 6.90(1H, d, J=8.1 Hz) 5.69(2H, d, J=9.4 Hz) 4.0-4.2(2H, m) 3.85(3H, s) 3.7-3.9(1H, m) 3.6-3.7(1H, m) 3.15(1H, d, J=9.4 Hz) 3.08(2H, q, J=6.6 Hz) 1.7-1.8(2H, m)		FAB+ 415 [M+H] ⁺ (60), 397(80), 179(100).	
7-55	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.37(1H, d, J=8.4 Hz) 7.11(1H, dd, J=5.1, 1.2 Hz) 6.92(1H, d, J=8.4 Hz) 6.89(1H, dd, J=5.1, 3.3 Hz) 6.83(1H, dd, J=3.3, 1.2 Hz) 5.65(1H, d, J=9.9 Hz) 4.0-4.1(2H, m) 3.87(3H, s) 3.80(1H, q, J=6.9 Hz) 3.61(1H, qul, J=6.9 Hz) 3.47(1H, d, J=4.5 Hz) 3.17(2H, t, J=7.2 Hz)	KBr 3312 1672 1267	FAB+ 376 [M+H] ⁺ (50), 358(100).	
7-56	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 7.40(1H, d, J=8.1 Hz) 7.12(1H, d, J=8.1 Hz) 7.07(2H, d, J=8.1 Hz) 6.94(1H, d, J=8.1 Hz) 5.61(1H, d, J=9.5 Hz) 4.0-4.2(2H, m) 3.87(3H, s) 3.80(1H, q, J=6.9 Hz) 3.60(2H, q, J=6.9 Hz) 2.93(2H, t, J=7.2 Hz) 2.68(1H, d, J=9.8 Hz) 2.30(3H, s)		FAB+ 384[M+H] ⁺ (100), 366(100).	

Table 129

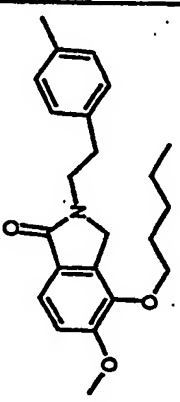
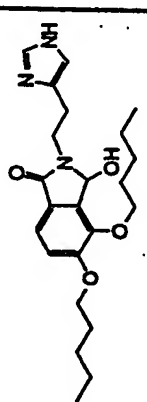
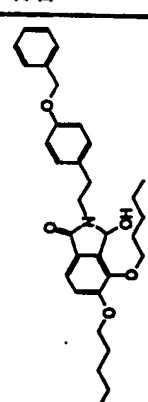
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-57	 <p>Colorless crystals</p>	57.4-58.5 °C	CDCl ₃ , 300MHz 7.52 (1H, d, J = 8.1 Hz) 7.13 (2H, d, J = 8.1 Hz) 7.08 (2H, d, J = 8.1 Hz) 6.98 (1H, d, J = 8.1 Hz) 4.17 (2H, s) 4.01 (2H, t, J = 6.9 Hz) 3.90 (3H, s) 3.80 (2H, t, J = 7.2 Hz) 2.99 (2H, t, J = 7.2 Hz) 1.7-1.8 (2H, m) 1.3-1.5 (4H, m) 0.93 (3H, t, J = 7.2 Hz)		FAB+ 368[M+H+] (100)	
7-58				Neat 3500 2956 1769 1274	FAB+ 416 [M+H] ⁺ (10) 398(100)	
7-59	 <p>Colorless crystals</p>	108.2 ~ 108.4 °C	CDCl ₃ , 300MHz 7.3-7.5 (5H, m) 7.39 (1H, d, J = 8.6 Hz) 7.14 (2H, d, J = 8.6 Hz) 6.91 (1H, d, J = 8.6 Hz) 6.88 (2H, d, J = 8.6 Hz) 5.65 (1H, d, J = 9.8 Hz) 5.02 (2H, s) 4.0-4.2 (2H, m) 3.99 (2H, t, J = 6.5 Hz) 3.7-3.9 (1H, m) 3.5-3.6 (1H, m) 2.91 (2H, t, J = 6.8 Hz)	KBr 3252 2951 1659 1271	FAB+ 531 [M+H] ⁺ (20) 514(80) 165(100)	C ₂₃ H ₂₁ NO ₃ Calcd. C: 74.55% H: 7.77% N: 2.63% Found C: 74.82% H: 7.77% N: 2.67%

Table 130

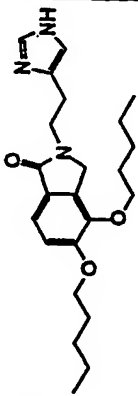
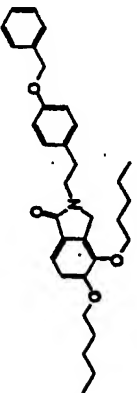
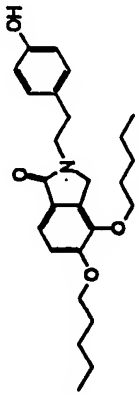
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-60	 <p>Colorless crystals</p>	114.2~ 114.6°C	CDCl ₃ , 300MHz 7.61(1H, s) 7.45(1H, d, J=8.3 Hz) 6.97(1H, t, J=8.3 Hz) 6.86(1H, s) 4.60(1H, bs) 4.31(2H, s) 4.07(2H, t, J=6.6 Hz) 4.04(2H, t, J=6.5 Hz) 3.91(2H, t, J=6.8 Hz) 3.04(2H, t, J=6.8 Hz) 1.8-1.9(2H, m) 1.7-1.8(2H, m)	Neat 3238 2926 1660 1464 1268	FAB+ 400 [M ⁺ H] ⁺ (100)	
7-61	 <p>Colorless oil</p>		CDCl ₃ , 300MHz 7.50(1H, d, J=8.2 Hz) 7.3-7.5(5H, m) 7.16(2H, d, J=8.6 Hz) 6.97(1H, d, J=8.2 Hz) 6.90(2H, d, J=8.6 Hz) 5.03(2H, s) 4.19(2H, s) 4.05(2H, t, J=6.6 Hz) 4.04(2H, t, J=6.5 Hz) 3.80(2H, t, J=7.6 Hz) 2.93(2H, t, J=7.6 Hz) 1.8-1.9(2H, m)	Neat 2931 1687 1618 1511 1271	FAB+ 516 [M ⁺ H] ⁺ (100) 318(50)	C ₂₃ H ₂₁ NO ₂ Calcd. C: 76.86% H: 8.01% N: 2.72% Found C: 76.26% H: 8.17% N: 2.43%
7-62	 <p>Colorless needles</p>	122.2~ 122.6°C	CDCl ₃ , 300MHz 7.49(1H, d, J=8.3 Hz) 7.06(2H, d, J=8.5 Hz) 6.95(1H, d, J=8.3 Hz) 6.75(2H, d, J=8.5 Hz) 6.72(1H, bs) 4.24(2H, s) 4.06(2H, t, J=6.7 Hz) 4.02(2H, t, J=6.5 Hz) 3.83(2H, t, J=7.2 Hz) 2.91(2H, t, J=7.2 Hz) 1.8-1.9(2H, m) 1.7-1.8(2H, m)	KBr 3156 2932 1657 1464 1273	FAB+ 426 [M ⁺ H] ⁺ (100)	C ₂₄ H ₂₃ NO ₂ Calcd. C: 73.38% H: 8.29% N: 3.29% Found C: 73.60% H: 8.30% N: 3.29%

Table 131

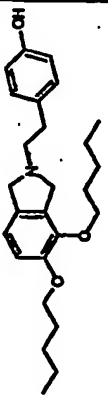
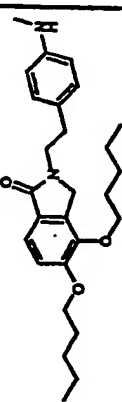
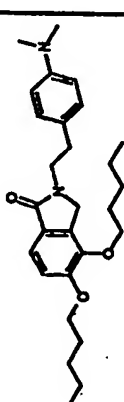
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm ⁻¹	MS	Elem. anal.
7-63	 <p>Colorless crystals</p>	78.3~ 78.6°C	CDCl ₃ , 300MHz 7.08 (2H, d, J = 8.5 Hz) 6.82 (1H, d, J = 8.1 Hz) 6.75 (1H, d, J = 8.1 Hz) 6.68 (2H, d, J = 8.5 Hz) 3.9-4.1 (8H, m) 2.9-3.0 (2H, m) 2.9-2.9 (2H, m) 1.7-1.9 (4H, m) 1.3-1.5 (8H, m) 0.93 (3H, t, J = 7.0 Hz) 0.92 (3H, t, J = 7.0 Hz)	KBr 3500 2932 1613 1515 1490 1263	FAB+ 412[M+H+] (100)	
7-64	 <p>Colorless crystals</p>	91.7~ 92.0°C	CDCl ₃ , 300MHz 7.50 (1H, d, J = 8.2 Hz) 7.06 (2H, d, J = 8.4 Hz) 6.97 (1H, d, J = 8.2 Hz) 6.54 (2H, d, J = 8.4 Hz) 4.19 (2H, s) 4.05 (2H, t, J = 6.6 Hz) 4.04 (2H, t, J = 6.6 Hz) 3.76 (2H, t, J = 7.1 Hz) 3.60 (1H, br) 2.86 (2H, t, J = 7.1 Hz) 2.81 (3H, s) 1.8-1.9 (2H, m)		FAB+ 439[M+H+] (100)	C ₂₇ H ₃₈ N ₂ O ₃ Calcd. C: 73.94% H: 8.73% N: 6.39% Found C: 73.89% H: 9.10% N: 6.41%
7-65	 <p>Colorless oil</p>		CDCl ₃ , 300MHz 7.50 (1H, d, J = 8.2 Hz) 7.10 (2H, d, J = 8.7 Hz) 6.98 (1H, d, J = 8.2 Hz) 6.58 (2H, d, J = 8.7 Hz) 4.20 (2H, s) 4.03 (4H, t, J = 6.6 Hz) 3.78 (2H, t, J = 7.1 Hz) 2.90 (6H, s) 2.88 (2H, t, J = 7.1 Hz) 1.8-1.9 (2H, m) 1.6-1.8 (2H, m) 1.3-1.5 (8H, m)	Neat 3280 2931 2870 1666 1617 1523 1273	FAB+ 453[M+H+] (100)	

Table 132

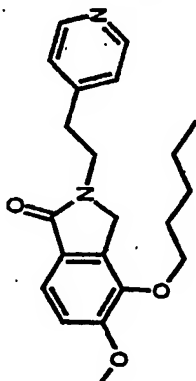
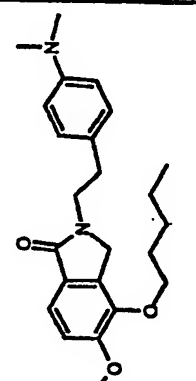
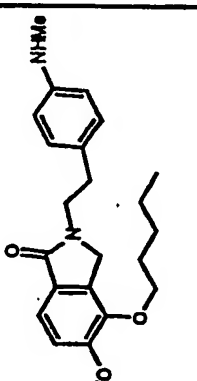
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-66	 <p>Amorphous</p>		CDCl ₃ , 300MHz 8.51 (2H, d, J = 6.0 Hz) 7.53 (1H, d, J = 8.4 Hz) 7.19 (2H, d, J = 6.0 Hz) 7.00 (1H, d, J = 8.4 Hz) 4.23 (2H, s) 4.04 (2H, t, J = 6.6 Hz) 3.91 (3H, s) 3.87 (2H, t, J = 7.2 Hz) 3.00 (2H, t, J = 7.2 Hz) 1.7-1.8 (2H, m) 1.3-1.5 (4H, m) 0.94 (3H, t, J = 7.2 Hz)		FAB+ 355[M+H+] (100).	
7-67	 <p>Amorphous</p>		CDCl ₃ , 300MHz 7.53 (1H, d, J = 8.1 Hz) 7.11 (2H, d, J = 8.4 Hz) 6.99 (1H, d, J = 8.1 Hz) 6.68 (2H, d, J = 8.4 Hz) 4.20 (2H, s) 4.01 (2H, t, J = 6.9 Hz) 3.90 (3H, s) 3.78 (2H, t, J = 7.2 Hz) 2.91 (6H, s) 2.88 (1H, d, J = 6.9 Hz) 1.5-1.8 (2H, m) 1.3-1.5 (4H, m)	Neat 2926 1682 1615 1522 1494 1270 1076	FAB+ 397 [M+H+](30), 147(100).	
7-68	 <p>Amorphous</p>		CDCl ₃ , 300MHz 7.52 (1H, d, J = 8.1 Hz) 7.05 (2H, d, J = 8.4 Hz) 6.99 (1H, d, J = 8.1 Hz) 6.54 (2H, d, J = 8.4 Hz) 4.36 (1H, s) 4.21 (2H, s) 4.02 (2H, t, J = 6.6 Hz) 3.90 (3H, s) 3.77 (2H, t, J = 7.2 Hz) 2.87 (1H, t, J = 7.2 Hz) 2.81 (3H, s) 1.6-1.8 (2H, m)	Neat 2931 1650 1622 1595 1524 1484 1282	FAB+ 383[M+H+] (100).	

Table 133

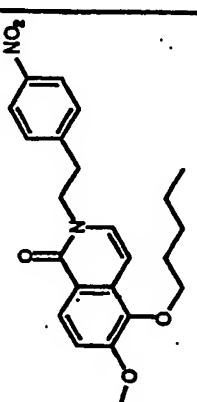
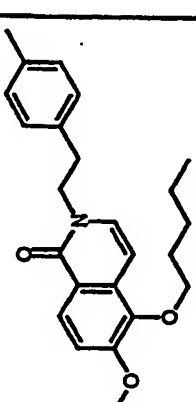
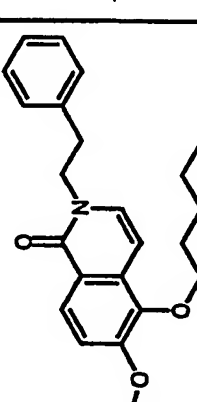
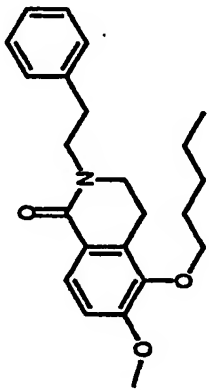
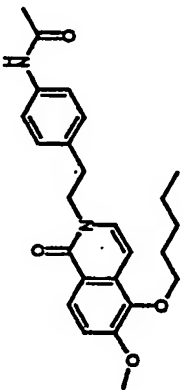
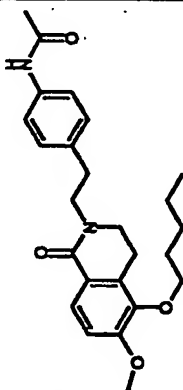
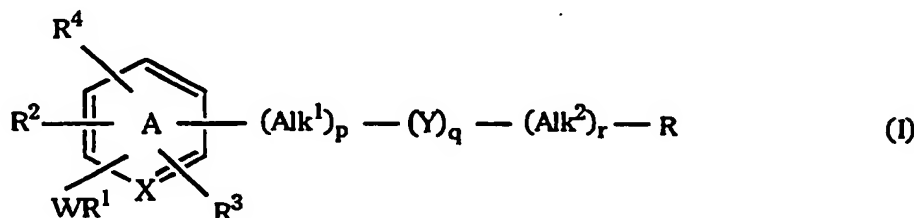
Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IR cm^{-1}	MS	Elem. anal.
7-69	 <p>Pale-green solid</p>		CDCl ₃ , 300MHz 8.17 (1H, d, J = 8.8 Hz) 8.14 (1H, d, J = 8.8 Hz) 7.36 (2H, d, J = 8.8 Hz) 7.14 (1H, d, J = 8.8 Hz) 6.75 (1H, d, J = 7.5 Hz) 6.67 (1H, d, J = 7.5 Hz) 4.20 (2H, t, J = 7.2 Hz) 4.01 (2H, d, J = 6.8 Hz) 3.96 (3H, s) 3.20 (2H, t, J = 7.2 Hz) 1.7-1.9 (2H, m) 1.4-1.6 (4H, m)		FAB+ 380[M+H+] (100), 119 (50).	
7-70	 <p>Colorless solid</p>		CDCl ₃ , 300MHz 8.19 (1H, d, J = 8.8 Hz) 7.12 (1H, d, J = 8.8 Hz) 7.09 (4H, s) 6.78 (1H, d, J = 7.5 Hz) 6.65 (1H, d, J = 7.5 Hz) 4.14 (2H, t, J = 7.2 Hz) 4.01 (2H, t, J = 6.6 Hz) 3.96 (3H, s) 3.02 (2H, t, J = 7.2 Hz) 2.31 (3H, s) 1.7-1.9 (2H, m) 1.3-1.5 (4H, m)		FAB+ 380[M+H+] (100), 119 (50).	
7-71	 <p>Colorless oil</p>		CDCl ₃ , 300MHz 8.20 (1H, d, J = 9.0 Hz) 7.2-7.4 (5H, m) 7.13 (1H, d, J = 9.0 Hz) 6.76 (1H, d, J = 7.5 Hz) 6.64 (1H, d, J = 7.5 Hz) 4.17 (2H, t, J = 7.5 Hz) 4.00 (2H, t, J = 6.6 Hz) 3.96 (3H, s) 3.07 (2H, t, J = 7.5 Hz) 1.7-1.9 (2H, m) 1.3-1.5 (4H, m) 0.93 (3H, t, J = 7.5 Hz)		FAB+ 366[M+H+] (100), 261 (50).	

Table 134

Ex.	Structural formula	m.p.	¹ H NMR (δ) ppm	IRcm ⁻¹	MS	Elem. anal.
7-72	 <p>Colorless oil</p>		CDCl ₃ , 300MHz 7.84 (1H, d, J = 9.0 Hz) 7.2-7.4 (5H, m) 6.86 (1H, d, J = 9.0 Hz) 3.89 (2H, t, J = 6.6 Hz) 3.87 (3H, s) 3.76 (2H, t, J = 7.5 Hz) 3.34 (2H, t, J = 6.6 Hz) 2.95 (2H, t, J = 7.5 Hz) 2.86 (2H, t, J = 6.6 Hz) 1.7-1.8 (2H, m) 1.3-1.5 (4H, m) 0.92 (3H, t, J = 7.5 Hz)		FAB+ 368[M+H+] (100), 276 (50).	
7-73	 <p>Colorless crystals</p>		CDCl ₃ , 300MHz 8.19 (1H, d, J = 9.0 Hz) 7.41 (2H, d, J = 8.4 Hz) 7.15 (2H, d, J = 8.4 Hz) 7.12 (2H, d, J = 8.4 Hz) 6.76 (1H, d, J = 7.5 Hz) 6.64 (1H, d, J = 7.5 Hz) 4.41 (2H, t, J = 7.5 Hz) 4.00 (2H, t, J = 6.6 Hz) 3.96 (3H, s) 3.07 (2H, t, J = 7.5 Hz) 2.16 (3H, s) 1.7-1.8 (2H, m) 1.3-1.5 (4H, m) 0.93 (3H, t, J = 7.5 Hz)		FAB+ 423[M+H+] (100)	
7-74	 <p>Pale-yellow crystals</p>		CDCl ₃ , 300MHz 7.82 (1H, d, J = 8.7 Hz) 7.42 (2H, d, J = 8.4 Hz) 7.19 (2H, d, J = 8.4 Hz) 6.86 (1H, d, J = 8.7 Hz) 3.90 (2H, t, J = 6.9 Hz) 3.88 (3H, s) 3.73 (2H, t, J = 7.2 Hz) 3.36 (2H, t, J = 6.6 Hz) 2.89 (4H, q, J = 6.6 Hz) 2.16 (3H, s) 1.7-1.8 (2H, m) 1.3-1.5 (4H, m)		FAB+ 425[M+H+] (100), 276(40).	

WHAT IS CLAIMED IS

1. A cannabinoid receptor activator or antagonist comprising, as an active ingredient, a compound of the formula (I)



wherein

X is CH or N;

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-
wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl

wherein

each group at R¹ is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R² is a hydrogen atom, an alkyl, -OR¹⁰ wherein R¹⁰ is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, or R⁸ and R⁹ optionally form heteroaryl together with the adjacent nitrogen atom, or -(CH₂)_uS(O)_{u'}R¹² wherein R¹² is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

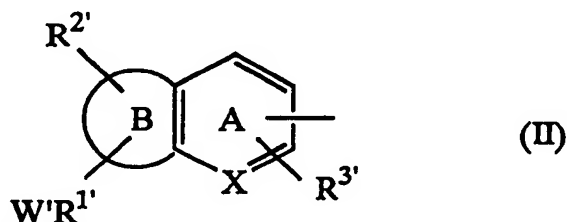
wherein

each group at said R² except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy,

alkoxycarbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a carboxyl, an alkoxy-carbonyl, a halogen atom or nitro, said alkyl being optionally substituted by alkoxy or hydroxy;

R^4 is a hydrogen atom, or R^4 and R^2 form, together with A ring, a condensed ring of the formula (II)



wherein $W'R^1$, $R^{2'}$ and $R^{3'}$ are substituted at an optional position of A ring or B ring, $W'R^1$, $R^{2'}$ and $R^{3'}$ are each as defined above for WR^1 , R^2 and R^3 , respectively, and B ring is a benzene ring, pyridine ring or furan ring;

Alk^1 is $-CH=CH-$, $-CH_2CH_2-$ or $-C\equiv C-$;

Y is $-CONR^{10}-$, $-NR^{11}CO-$, $-COO-$, $-CH_2NR^{10}-$ or $-NHCONH-$ wherein,

R^{10} and R^{11} are the same or different and each is hydrogen atom, alkyl, alkenyl or amino-protecting group, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxycarbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form

heteroaryl together with the adjacent nitrogen atom;
 R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, pyridyl, piperidino, carboxyl, alkoxy carbonyl, acylamino, aminocarbonyl or cyano, said cycloalkyl is optionally substituted by hydroxy, alkoxy or =O, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

p, q and r are each independently 0 or 1,

provided that

when p=1 and q=1, Alk^1 is $-\text{CH}=\text{CH}-$, Y is $-\text{CONR}^{10}-$, and R^3 and R^{10} in combination optionally show $-\text{NHCO}-$ to form a condensed ring with A ring,

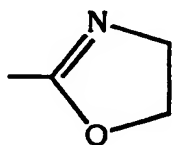
when p=0 and q=1, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R^3 and R^{10} in combination optionally show $-\text{CH}=\text{CH}-$, $-\text{CH}_2\text{CHR}^{27}-$, $-\text{CH}_2-$, $-\text{S}-$, $-\text{CHOH}-$, $-\text{CO}-$, $-\text{CH}_2\text{CO}-$, $-\text{NHCR}^{28}(\text{CH}_2)_{v'}-$, $-\text{NHCR}^{29}\text{R}^{30}-$ or $-\text{N}=\text{CR}^{31}-$ to form a condensed ring with A ring wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl,

R^{31} is alkyl or hydrogen atom and v' is 0 or 1,

when r=0 and q=1, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R and R^{10} optionally form heteroaryl together with the adjacent nitrogen atom, and

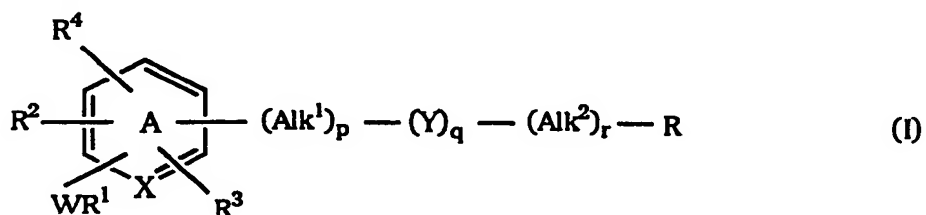
when p=q=r=0, R is a group of the formula (i)



(i)

wherein said group is optionally substituted by alkyl optionally substituted by hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkyl-amino, aralkyloxy or pyridyl;
or a pharmaceutically acceptable salt thereof.

2. The cannabinoid receptor activator or antagonist of claim 1, comprising, as an active ingredient, a compound of the formula (I)



wherein

X is CH or N;

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO- or -CONR⁷-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl
wherein

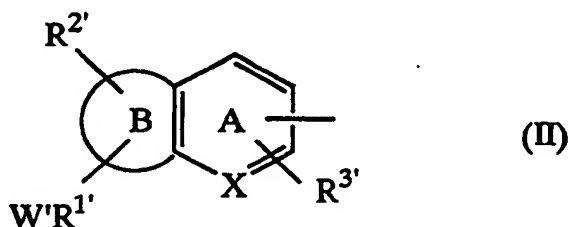
each group at R¹ is optionally substituted by alkyl, alkylamino or hydroxy;

R² is a hydrogen atom, an alkyl, -OR¹⁰ wherein R¹⁰ is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom, alkyl or acyl, or -(CH₂)_u-S(O)_{u'}-R¹² wherein R¹² is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2
wherein

each group at said R² except hydrogen atom is optionally substituted by alkyl, alkylamino or hydroxy;

R³ is a hydrogen atom, an alkoxy, an alkyl, an alkoxy carbonyl, a halogen atom or nitro, said alkyl being optionally substituted by hydroxy;

R^4 is a hydrogen atom, or R^4 and R^2 form, together with A ring, a condensed ring of the formula (II)



wherein $W'R^{1'}$, $R^{2'}$ and $R^{3'}$ are substituted at an optional position of A ring or B ring, $W'R^{1'}$, $R^{2'}$ and $R^{3'}$ are each as defined above for WR^1 , R^2 and R^3 , respectively, and B ring is a benzene ring or furan ring;

Alk^1 is $-CH=CH-$ or $-CH_2CH_2-$;

Y is $-CONR^{10}-$, $-NR^{11}CO-$, $-COO-$, $-CH_2NR^{10}-$ or $-NHCONH-$ wherein

R^{10} and R^{11} are the same or different and each is hydrogen atom, alkyl, alkenyl or amino-protecting group, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxycarbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by

alkyl, hydroxy, alkoxy, alkenyloxy, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, piperidino, carboxyl, acylamino, aminocarbonyl or cyano, said cycloalkyl is optionally substituted by hydroxy or =O, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy; and

p, q and r are each independently 0 or 1,

provided that

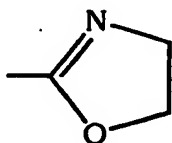
when $p=0$ and $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R^3 and R^{10} in combination optionally show $-\text{CH}=\text{CH}-$, $-\text{CH}_2\text{CHR}^{27}-$, $-\text{CH}_2-$, $-\text{S}-$, $-\text{CHOH}-$, $-\text{CO}-$, $-\text{CH}_2\text{CO}-$, $-\text{NHCR}^{28}(\text{CH}_2)_{v'}-$, $-\text{NHCR}^{29}\text{R}^{30}-$ or $-\text{N}=\text{CR}^{31}-$ to form a condensed ring with A ring wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl,

R^{31} is alkyl or hydrogen atom and v' is 0 or 1,

when $r=0$ and $q=1$, Y is $-\text{CONR}^{10}-$ or $-\text{CH}_2\text{NR}^{10}-$, and R and R^{10} optionally form heteroaryl together with the adjacent nitrogen atom, and

when $p=q=r=0$, R is a group of the formula (i)



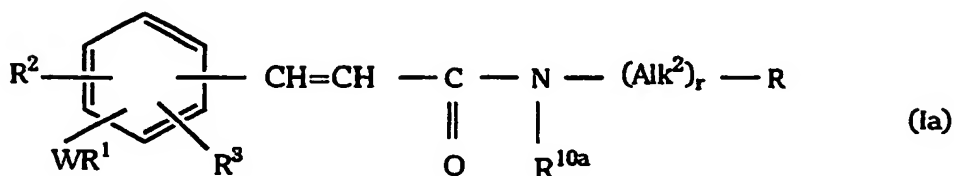
(i)

wherein said group is optionally substituted by alkyl or pyridyl; or a pharmaceutically acceptable salt thereof.

3. (deleted)

4. (deleted)

5. (amended) A compound of the formula (Ia)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶- or -NR⁷-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl wherein

each group at R¹ is optionally substituted by alkyl or alkylamino;

R² is a hydrogen atom, an alkyl, -OR¹⁵ wherein R¹⁵ is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, -NR⁸R⁹ wherein R⁸ and R⁹ are the same or different and each is hydrogen atom or alkyl, or -(CH₂)_u-S(O)_{u'}R¹² wherein R¹² is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2 wherein

each group at said R² except hydrogen atom is optionally substituted by alkyl or alkylamino;

R³ is a hydrogen atom or an alkoxy;

R^{10a} is a hydrogen atom or an alkyl, said alkyl being optionally substituted by heteroaryl;

Alk² is an alkylene

wherein

said alkylene is optionally substituted by alkoxycarbonyl, alkyl optionally substituted by hydroxy, or -CONR¹³R¹⁴ wherein R¹³ and R¹⁴ are the same or different and each is hydrogen atom or alkyl;

R is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl,

hydroxy, alkoxy, alkenyloxy, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino or cyano, said cycloalkyl is optionally substituted by hydroxy, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

wherein R² is substituted at the para position on the benzene ring and -WR¹ is substituted at the meta position on the benzene ring, both relative to the binding site of -CH=CH-CO-NR^{10a}-(Alk²)_r-R on the benzene ring, provided that when r=0, R and R^{10a} optionally form morpholino or imidazolyl together with the adjacent nitrogen atom;

or a pharmaceutically acceptable salt thereof.

6. The compound of claim 5, wherein R¹ is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

7. The compound of claim 6, wherein Alk² is ethylene, or a pharmaceutically acceptable salt thereof.

8. (amended) The compound of claim 5, wherein, when r=0, R and R^{10a} form morpholino together with the adjacent nitrogen atom, or a pharmaceutically acceptable salt thereof.

9. The compound of claim 7, which is selected from the group consisting of

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

3-(4-ethoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]-acrylamide,

3-(3,4-dipentyloxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-butyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-hexyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-heptyloxyphenyl)-acrylamide,

(E)-N-[2-(3-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(2-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxycyclohexyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-N-methyl-3-(4-methoxy-3-pentyloxyphenyl)acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-isopentyloxy-4-methoxyphenyl)-acrylamide,

3-[3-(2-ethylbutyloxy)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)acrylamide,

3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(3,4-dihydroxyphenyl)ethyl]-3-[3-(1,1-dimethylheptyl)-4-methoxyphenyl]acrylamide,

3-(3-hexyl-4-methoxyphenyl)-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-(4-amino-3-pentyloxyphenyl)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-(4-amino-3-pentyloxyphenyl)-N-[2-(4-nitrophenyl)ethyl]acrylamide,

3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-pentyloxyphenyl)ethyl]-acrylamide,

(E)-N-[2-(4-methoxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-(2-morpholinoethyl)acrylamide,

(E)-N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,

2-[2-{3-(3-pentyloxy-4-methoxyphenyl)acryloylamino}ethyl]pyridine-N-oxide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-acrylamide,

3-[3-(N',N'-dipentylamino)-4-methoxyphenyl]-(E)-N-[2-(4-hydroxyphenyl)ethyl]acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentylamino-4-pentyloxyphenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-[3-(N'-methyl-N'-pentylamino)-4-methoxyphenyl]acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-pentyloxy-3-pentylthiophenyl)-acrylamide,

(E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentyloxy-4-pentylthiophenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(3-pentyloxy-4-methylthiophenyl)-acrylamide,

(E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-acrylamide,

(E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-acrylamide,

(E)-N-[2-(imidazol-4-yl)ethyl]-3-(4-methoxy-3-pentylthiophenyl)-acrylamide,

(E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-acrylamide,

(E)-N-[2-(imidazol-4-yl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-acrylamide,

(E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-methylamino-3-pentyloxyphenyl)acrylamide,

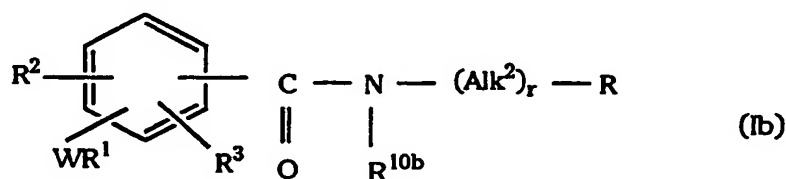
(E)-N-[2-(4-aminophenyl)ethyl]-3-(4-methoxy-3-pentylaminophenyl)-acrylamide,

(E)-N-[2-(4-nitrophenyl)ethyl]-3-(4-methylamino-3-pentyloxyphenyl)-acrylamide,
 3-(4-methoxy-3-pentyloxyphenyl)-(E)-N-[2-(4-thiophen-2-yl)ethyl]-acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-[(N'-methyl-N'-pentylamino)-4-pentyloxyphenyl]acrylamide,
 (E)-N-[2-(4-hydroxyphenyl)ethyl]-3-(4-pentylamino-3-pentyloxyphenyl)-acrylamide,
 (E)-N-[2-(4-cyanophenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide and
 (E)-N-[2-(4-carbamoylphenyl)ethyl]-3-(4-methoxy-3-pentyloxyphenyl)-acrylamide,
 or a pharmaceutically acceptable salt thereof.

10. (deleted)

11. (deleted)

12. (amended) A compound of the formula (Ib)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷- or -NR⁷CO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl, an alkenyl, an alkynyl, an arylalkyl or a cycloalkylalkyl
 wherein

each group at R¹ is optionally substituted by alkyl, alkylamino or

hydroxy;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, arylalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl or acyl, or $-(CH_2)_uS(O)_uR^{12}$ wherein R^{12} is alkyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino or hydroxy;

R^3 is a hydrogen atom, an alkoxy, an alkyl, a nitro or a halogen atom, said alkyl being optionally substituted by hydroxy;

R^{10b} is a hydrogen atom, an alkyl or an alkenyl, said alkyl being optionally substituted by heteroaryl, arylsulfinyl or alkoxy carbonyl, and said alkenyl being optionally substituted by phenylthio;

Alk^2 is an alkylene or an alkenylene

wherein

said alkylene and alkenylene are each optionally substituted by hydroxy, carboxyl, alkoxy carbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-CONR^{13}R^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl;

R is an aryl, a heteroaryl except pyridyl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl, hydroxy, alkenyloxy, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino or aralkyloxy, said cycloalkyl is optionally substituted by hydroxy, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy; and

r is 0 or 1,

wherein R^2 is substituted at the para-position on the benzene ring and $-WR^1$ is substituted at the meta-position on the benzene ring, both relative to the binding site of $-CO-NR^{10b}-(Alk^2)_r-R$ on the benzene ring,

provided that when $r=0$, R and R^{10b} optionally form morpholino or imidazolyl together with the adjacent nitrogen atom; or a pharmaceutically acceptable salt thereof.

13. The compound of claim 12, wherein R¹ is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13, wherein Alk² is ethylene, or a pharmaceutically acceptable salt thereof.

15. The compound of claim 14, which is selected from the group consisting of
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 4-ethoxy-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,
 3,4-dipentyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 4-dimethylamino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentylamino-4-methoxybenzamide,
 3-butyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-hexyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-heptyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(3-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(2-hydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxycyclohexyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-N-methyl-4-methoxy-3-pentyloxybenzamide,
 3-isopentyloxy-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 3-(2-ethylbutyloxy)-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-4-hydroxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxy-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxy-N-methyl-3-pentyloxybenzamide,
 3-(1,1-dimethylheptane)-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(1,1-dimethylheptane)-4-methoxybenzamide,
 3-(1,1-dimethylheptane)-N-[2-(4-hydroxy-3-methoxyphenyl)ethyl]-4-

methoxybenzamide,

3-(1,1-dimethylheptane)-N-[2-(4-hydroxyphenyl)ethyl]-4-hydroxybenzamide,
 N-[2-(3,4-dihydroxyphenyl)ethyl]-3-(1,1-dimethylheptane)-4-hydroxybenzamide,
 3-hexyl-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(4-aminophenyl)ethyl]-3,4-dipentyloxybenzamide,
 3,4-dihexyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 4-methoxy-N-[2-(4-pentyloxyphenyl)ethyl]-3-pentyloxybenzamide,
 4-methoxy-N-(2-morpholinoethyl)-3-pentyloxybenzamide,
 4-methoxy-N-[2-(4-propen-2-yloxyphenyl)ethyl]-3-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-N-[2-(phenylsulfinyl)ethyl]-3-

pentyloxybenzamide,

N-[2-(3,4-dihydroxyphenyl)ethyl]-4-methoxy-3-pentyloxybenzamide,
 N-[2-(4-acetoxyphenyl)ethyl]-4-methoxy-3-pentyloxy-N-(E)-

phenylthiovinylbenzamide,

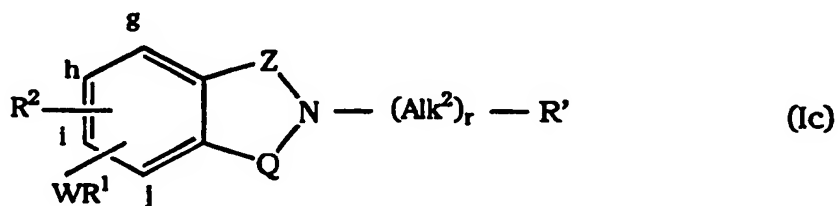
N-[2-(4-acetoxyphenyl)ethyl]-N-ethyl-4-methoxy-3-pentyloxybenzamide,
 4-[2-{N-(4-methoxy-3-pentyloxybenzoyl)amino}ethyl]pyridine-N-oxide,
 3-[2-{N-(4-methoxy-3-pentyloxybenzoyl)amino}ethyl]pyridine-N-oxide,
 3-dipentylamino-N-[2-(4-hydroxyphenyl)ethyl]-4-methoxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-isohexyl-4-methoxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-(N'-methyl-N'-pentylamino)-

benzamide,

N-[2-(4-hydroxyphenyl)ethyl]-3-pentylamino-4-pentyloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-pentylamino-3-pentyloxybenzamide,
 3,4-dipentyloxy-N-[2-(4-sulfamoylphenyl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(imidazol-4-yl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(4-nitrophenyl)ethyl]benzamide,
 3,4-dipentyloxy-N-[2-(4-fluorophenyl)ethyl]benzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentyloxy-4-propen-2-ylbenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-propyloxy-3-pentyloxybenzamide,
 3,4-dibutyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 3,4-diheptyloxy-N-[2-(4-hydroxyphenyl)ethyl]benzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methylamino-3-pentyloxybenzamide,

N-[2-(4-hydroxyphenyl)ethyl]-3,4-dipentylaminobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-(N'-methyl-N'-pentylamino)-4-pentylloxybenzamide,
 4-amino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentylloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-pentylloxy-3-pentylthiobenzamide,
 3,4-dipentylloxy-N-[2-(2-thienyl)ethyl]benzamide,
 3,4-dipentylloxy-N-[2-(5-hydroxyindol-3-yl)ethyl]benzamide,
 3,4-dipentylloxy-N-[2-(4-methylaminophenyl)ethyl]benzamide,
 N-[2-(4-dimethylaminophenyl)ethyl]-3,4-dipentylloxybenzamide,
 4-butyrylamino-N-[2-(4-hydroxyphenyl)ethyl]-3-pentylloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-formylamino-3-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-4-methylthio-3-pentylloxybenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-pentylloxy-4-pentylthiobenzamide,
 N-[2-(4-hydroxyphenyl)ethyl]-3-(4-hydroxybutyloxy)-4-methoxybenzamide,
 N-[2-(4-aminophenyl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 4-methoxy-N-[2-(4-nitrophenyl)ethyl]-3-pentylthiobenzamide,
 N-[2-(imidazol-4-yl)ethyl]-4-methoxy-3-pentylthiobenzamide,
 N-[2-(4-aminophenyl)ethyl]-4-pentylloxy-3-pentylthiobenzamide,
 N-[2-(4-nitrophenyl)ethyl]-4-pentylloxy-3-pentylthiobenzamide and
 N-[2-(imidazol-4-yl)ethyl]-4-pentylloxy-3-pentylthiobenzamide,
 or a pharmaceutically acceptable salt thereof.

16. (amended) A compound of the formula (Ic)



wherein

W is -O-, -S(O)_ε-, -CR⁵R⁶-, -NR⁷-, -NR⁷CO-, -CONR⁷-, -COO- or -OCO-

wherein

R^5 and R^6 are the same or different and each is hydrogen atom or alkyl, R^7 is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^1 is an alkyl, an alkenyl, an alkynyl, an aryl, an arylalkyl, a heteroaryl, a heteroarylalkyl, a cycloalkyl or a cycloalkylalkyl wherein

each group at R^1 is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

R^2 is a hydrogen atom, an alkyl, $-OR^{15}$ wherein R^{15} is hydrogen atom, alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, $-NR^8R^9$ wherein R^8 and R^9 are the same or different and each is hydrogen atom, alkyl, alkenyl, alkynyl, acyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl or cycloalkylalkyl, or R^8 and R^9 optionally form heteroaryl together with the adjacent nitrogen atom, or $-(CH_2)_uS(O)_uR^{12}$ wherein R^{12} is hydrogen atom, alkyl, alkenyl or alkynyl, u is 0, 1 or 2 and u' is 0, 1 or 2

wherein

each group at said R^2 except hydrogen atom is optionally substituted by alkyl, alkylamino, amino, hydroxy, alkoxy, alkoxy carbonyl, acyl, acyloxy, acylthio, mercapto, alkylthio, alkylsulfinyl or alkylsulfonyl;

Z is $-CH_2-$ or $-CO-$;

Q is $-CH=CH-$, $-CH_2CHR^{27}-$, $-CH_2-$, $-S-$, $-CHOH-$, $-CO-$, $-CH_2CO-$, $-NHCR^{28}(CH_2)_{v'}-$, $-NHCR^{29}R^{30}-$ or $-N=CR^{31}-$

wherein

R^{27} is hydrogen atom or hydroxy, R^{28} is oxygen atom or sulfur atom, R^{29} and R^{30} are the same or different and each is alkyl, R^{31} is alkyl or hydrogen atom and v' is 0 or 1;

Alk^2 is an alkylene, an alkenylene, $-COCH_2-$ or $-CONH(CH_2)_v-$ wherein v is 0, 1 or 2

wherein

alkylene and alkenylene at said Alk^2 are each optionally substituted by hydroxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted by hydroxy, alkoxy or alkylthio, or $-\text{CONR}^{13}\text{R}^{14}$ wherein R^{13} and R^{14} are the same or different and each is hydrogen atom or alkyl, or R^{13} and R^{14} optionally form heteroaryl together with the adjacent nitrogen atom;

R' is an aryl, a heteroaryl, a cycloalkyl or a benzene-condensed cycloalkyl

wherein

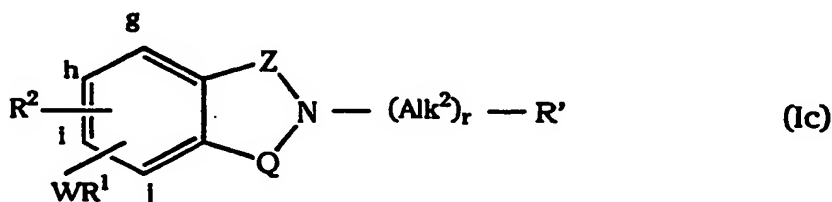
said aryl and heteroaryl are each optionally substituted by alkyl optionally substituted by hydroxy, hydroxy, alkoxy, alkenyloxy, acyl, acyloxy, halogen atom, nitro, amino, sulfonamide, alkylamino, aralkyloxy, acylamino, piperidino or pyridyl, said cycloalkyl is optionally substituted by hydroxy, alkoxy or $=\text{O}$, and said benzene-condensed cycloalkyl is optionally substituted by hydroxy or alkoxy; and

r is 0 or 1,

provided that when Z is $-\text{CO}-$ and Q is $-\text{NHCR}^{28}(\text{CH}_2)_{v'}-$ wherein R^{28} is oxygen atom and v' is 0, R^2 is substituted at the i -position on the benzene ring, and $-\text{WR}^1$ is substituted at the j -position on the benzene ring,

or a pharmaceutically acceptable salt thereof.

17. (amended) The compound of claim 16, which is represented by the formula (Ic)



wherein

W is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷- or -NR⁷CO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R¹ is an alkyl;

R² is a hydrogen atom, an alkyl or -OR¹⁵ wherein R¹⁵ is hydrogen atom or alkyl;

Z is -CH₂- or -CO-;

Q is -CH=CH-, -CH₂CHR²⁷-, -CH₂-, -S-, -CHOH-, -CO-, -CH₂CO-,
-NHCR²⁸(CH₂)_{v'}-, -NHCR²⁹R³⁰- or -N=CR³¹-

wherein

R²⁷ is hydrogen atom or hydroxy, R²⁸ is oxygen atom or sulfur atom, R²⁹ and R³⁰ are the same or different and each is alkyl, R³¹ is alkyl or hydrogen atom and v' is 0 or 1;

Alk² is an alkylene, -COCH₂- or -CONH(CH₂)_v- wherein v is 0, 1 or 2;

R' is an aryl, a heteroaryl or a cycloalkyl

wherein

said aryl and heteroaryl are each optionally substituted by alkyl, hydroxy, acyloxy, nitro, amino, alkylamino, aralkyloxy, acylamino or piperidino, and said cycloalkyl is optionally substituted by =O;

r is 0 or 1,

provided that when Z is -CO- and Q is -NHCR²⁸(CH₂)_{v'}- wherein R²⁸ is oxygen atom and v' is 0, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring,

or a pharmaceutically acceptable salt thereof.

18. The compound of claim 17, wherein Z is -CO- and Q is -CH₂-, or a pharmaceutically acceptable salt thereof.

19. The compound of claim 18, wherein R² is -OR¹⁵, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, or a pharmaceutically acceptable salt thereof.

20. The compound of claim 19, wherein R¹ is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

21. The compound of claim 20, which is selected from the group consisting of
 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-benzyloxyphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
 5-methoxy-2-[2-(4-nitrophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-methylphenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
 4,5-dipentyloxy-2-[2-(imidazol-4-yl)ethyl]-2,3-dihydroisoindol-1-one,
 2-[2-(4-benzyloxyphenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,
 4,5-dipentyloxy-2-[2-(4-nitrophenyl)ethyl]-2,3-dihydroisoindol-1-one,
 2-[2-(4-aminophenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,
 4,5-dipentyloxy-2-[2-(4-hydroxyphenyl)ethyl]-2,3-dihydroisoindol-1-one,
 4,5-dipentyloxy-2-[2-(4-methylaminophenyl)ethyl]-2,3-dihydroisoindol-1-one,
 2-[2-(4-dimethylaminophenyl)ethyl]-4,5-dipentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-aminophenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one,
 2-[2-(4-hydroxyphenyl)ethyl]-5-methoxy-4-pentylamino-2,3-dihydroisoindol-1-one,
 5-methoxy-4-pentyloxy-2-[2-(4-pyridine)ethyl]-2,3-dihydroisoindol-1-one,
 2-[2-(4-dimethylaminophenyl)ethyl]-5-methoxy-4-pentyloxy-2,3-dihydroisoindol-1-one and
 5-methoxy-2-[2-(4-methylaminophenyl)ethyl]-4-pentyloxy-2,3-dihydroisoindol-1-one,
 or a pharmaceutically acceptable salt thereof.

22. The compound of claim 17, wherein Z is -CO- and Q is -CH=CH-, or a pharmaceutically acceptable salt thereof.

23. The compound of claim 22, wherein R² is -OR¹⁵, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the

j-position on the benzene ring, or a pharmaceutically acceptable salt thereof.

24. The compound of claim 23, wherein R^1 is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

25. The compound of claim 24, which is selected from the group consisting of
 2-[2-(4-benzyloxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-pyridyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 4-[2-(6-methoxy-1-oxo-5-pentyloxy-1H-isoquinolin-2-yl)ethyl]phenyl acetate,
 6-methoxy-2-[2-(4-nitrophenyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-methylphenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 6-methoxy-5-pentyloxy-2-(2-phenylethyl)-2H-isoquinolin-1-one,
 2-[2-(4-acetylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 5,6-dipentyloxy-2-[2-(4-hydroxyphenyl)ethyl]-2H-isoquinolin-1-one,
 2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one
 hydrochloride,
 2-[2-(4-dimethylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 2-[2-(4-methylaminophenyl)ethyl]-6-methoxy-5-pentyloxy-2H-isoquinolin-1-one,
 6-methoxy-2-[2-(4-piperidinophenyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one
 and
 6-methoxy-2-[2-(4-pyridyl)ethyl]-5-pentyloxy-2H-isoquinolin-1-one
 hydrochloride,
 or a pharmaceutically acceptable salt thereof.

26. The compound of claim 17, wherein Z is -CO- and Q is -CH₂CHR²⁷- wherein R²⁷ is hydrogen atom, or a pharmaceutically acceptable salt thereof.

27. The compound of claim 26, wherein R² is -OR¹⁵, W is -O-, -NR⁷- or -NR⁷CO-, R²

is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, or a pharmaceutically acceptable salt thereof.

28. The compound of claim 27, wherein R¹ is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

29. The compound of claim 28, which is selected from the group consisting of

6-methoxy-2-[2-(4-oxocyclohexyl)ethyl]-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

4-[2-(6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-yl)-ethyl]phenyl aceate,

2-[2-(4-hydroxyphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-(2-phenylethyl)-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-acetylamino-phenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

6-hydroxy-2-[2-(4-hydroxyphenyl)ethyl]-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-methylphenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

2-[2-(4-aminophenyl)ethyl]-6-methoxy-5-pentyloxy-3,4-dihydro-2H-isoquinolin-1-one,

6-methoxy-5-pentyloxy-2-[2-(4-pyridyl)ethyl]-3,4-dihydro-2H-isoquinolin-1-one,

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-(4-aminophenyl)amide,

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-[(4-aminophenyl)methyl]amide and

6-methoxy-1-oxo-5-pentyloxy-3,4-dihydro-1H-isoquinolin-2-carboxylic acid N-(4-nitrophenyl)amide,

or a pharmaceutically acceptable salt thereof.

~~30. (deleted)~~

31 (amended) The compound of claim 17, wherein Z is -CO-, Q is -NHCR^{2a}(CH₂)_v- wherein R^{2a} is oxygen atom and v' is 0, R² is -OR^{1b}, W is -O-, -NR⁷- or -NR⁷CO-, R² is substituted at the i-position on the benzene ring, and -WR¹ is substituted at the j-position on the benzene ring, or a pharmaceutically acceptable salt thereof.

32. The compound of claim 31, wherein R¹ is alkyl having 4 to 6 carbon atoms, or a pharmaceutically acceptable salt thereof.

33. The compound of claim 32, which is selected from the group consisting of

7-methoxy-3-[2-(4-nitrophenyl)ethyl]-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

7-methoxy-3-[2-(4-pyridyl)ethyl]-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

3-[2-(4-aminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

3-[2-(4-hydroxyphenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

3-[2-(4-methylaminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione and

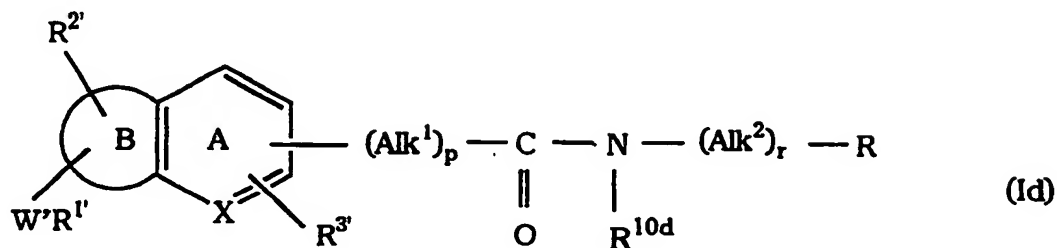
3-[2-(4-dimethylaminophenyl)ethyl]-7-methoxy-8-pentyloxy-(1H,3H)-quinazoline-2,4-dione,

or a pharmaceutically acceptable salt thereof.

~~34. (deleted)~~

~~35. (deleted)~~

36. (amended) A compound of the formula (Id)



wherein

X is N;

W' is -O-, -S(O)_t-, -CR⁵R⁶-, -NR⁷- or -NR⁷CO-

wherein

R⁵ and R⁶ are the same or different and each is hydrogen atom or alkyl, R⁷ is hydrogen atom or alkyl, and t is 0, 1 or 2;

R^{1'} is an alkyl;

R^{2'} is a hydrogen atom, an alkyl or -OR¹⁵ wherein R¹⁵ is hydrogen atom or alkyl;

R^{3'} is a hydrogen atom;

W'R^{1'}, R^{2'} and R^{3'} are substituted at an optional position of A ring or B ring, and B ring is a benzene ring or furan ring;

Alk¹ is -CH=CH- or -CH₂CH₂-;

R^{10d} is a hydrogen atom;

Alk² is an alkylene;

R is an aryl or a heteroaryl

wherein

said aryl and heteroaryl are each optionally substituted by hydroxy, nitro or amino; and

p and r are each independently 0 or 1,

or a pharmaceutically acceptable salt thereof.

37. The compound of claim 36, wherein R^{3'} is hydrogen atom, R^{2'} is -OR¹⁵, W is -O-, or a pharmaceutically acceptable salt thereof.

38. The compound of claim 37, wherein R^{1'} is alkyl having 4 to 6 carbon atoms, or

a pharmaceutically acceptable salt thereof.

39. The compound of claim 38, which is selected from the group consisting of

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-pyridyl)-ethyl]amide,

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-hydroxy-phenyl)ethyl]amide,

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-aminophenyl)-ethyl]amide,

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(4-nitrophenyl)-ethyl]amide and

7-methoxy-8-pentyloxyquinoline-3-carboxylic acid N-[2-(imidazol-4-yl)ethyl]amide,

or a pharmaceutically acceptable salt thereof.

~~40. (deleted)~~

~~41. (deleted)~~

~~42. (deleted)~~

~~43. (deleted)~~

~~44. (deleted)~~

45. (amended) A pharmaceutical composition comprising, as an active ingredient, any one of the compounds of claims 5-9, 12-29, 31-33 and 36-39, or a pharmaceutically acceptable salt thereof.

46. A cannabinoid receptor activator or antagonist of claim 1 or claim 2, wherein the cannabinoid receptor is a peripheral cannabinoid receptor.

47. (amended) The cannabinoid receptor activator or antagonist of any one of claim 1, claim 2 and claim 46, which is an immunoregulator, therapeutic agent for autoimmune diseases, antiinflammatory agent, antiallergic agent or therapeutic agent for nephritis.

48. (deleted)

49. (deleted)

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